

COCCIDIOSIS OF CATS AND DOGS AND THE STATUS OF THE *ISOСПORA* OF MAN

BY

C. M. WENYON

WELLCOME BUREAU OF SCIENTIFIC RESEARCH

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PLATES IX-XIV.

Our knowledge of the coccidia of dogs and cats commences with certain observations recorded by Finck (1854) on the changes undergone by the intestinal epithelium of cats during the process of food absorption. From that time to the present day it has been generally assumed that these animals harbour only one coccidium, which has been usually described during recent years under the name *Isospora bigemina* (Stiles, 1891). Though the measurements of the oocysts given by various observers who have studied the coccidia of these animals have differed considerably, the view that only one form exists has been rigidly adhered to with few exceptions. Perroncito (1882) appears to be the first to have considered it possible that more than one form occurred in these animals, for he separates the one described by Grassi (1879) from that recorded by Rivolta (1874-1878), while Neumann (1888), Railliet (1895) and Neveu-Lemaire (1912) seem to have held the same view. Dobell (1919, p. 177) states that there is no really conclusive evidence to prove that the *Isospora* of the cat is the same as that of the dog, or that both are merely varieties of one species, but he refers to all the coccidia of these animals by the name *Isospora bigemina*, pointing out, however, that Grassi's name *Coccidium Rivolta* has priority over that of Stiles. Reichenow (1921) definitely asserts that the form in the dog is probably distinct from that in the cat, while Nöller (1921), without giving any details, writes of a small and a large form in the cat.

Observations which have been made by the writer during the

past twelve months reveal the fact that there are at least three species of *Isospora* in these animals in England. One of these has an oocyst about 12-15 microns in length, another an oocyst about 25-30 microns in length, and a third an oocyst about 40-45 microns in length. The text-fig. 1 shows the relative size and appearance of the three types compared with the one discovered in man during the war. If these dimensions are kept in mind, the different accounts which have been given by various observers become at once intelligible, and it is possible to identify with some degree of certainty which form was actually under observation. All three have been previously recorded in the literature. In addition to the species of *Isospora*, dogs harbour an *Eimeria* with which we are not for the moment concerned.

HISTORICAL REVIEW OF LITERATURE

The first description of a coccidium of the cat was published by Finck (1854). His paper is difficult to obtain, but fortunately Davaine (1860) quotes in full the passage dealing with the bodies observed by this author. As it is of such importance from the present point of view it is quoted *in extenso* from Davaine, pp. 259-260.

"Sur le même animal (le chat) nous avons rencontré une autre forme bien plus singulière (fig. 22). Beaucoup de villosités, semblables du reste à celles chargées de graisse, à la place de gouttes graisseuses, renfermaient, en quantité considérable, des *corpuscules* que nous appellerons *gémînés*, parce que le plus souvent ils étaient réunis par paires. Tantôt une seule et même villosité offrait à la fois et des gouttes huileuses manifestes et des *corpuscules gémînés*, le tout entremêlé d'une manière irrégulière; tantôt les *corpuscules gémînés* remplissaient seuls le bout de la villosité. Ils étaient pour la plupart elliptiques, et leur grand diamètre atteignait à peine un centième de millimètre; la plupart mesuraient 0^{mm}, 08 sur 0^{mm}, 07, ou bien 0^{mm}, 1 sur 0^{mm}, 09. Leur contour était fin, net, très noir; leur contenu variable, occupant tantôt presque toute la cellule, plus souvent accumulé vers son centre. C'était une matière granuleuse réunie en une ou plusieurs masses. Il nous a semblé parfois voir une enveloppe commune pour deux corps gémînés.

"Quel est la nature de ces corps? Remak représente un corpuscule semblable au premier aspect, seulement plus grand et non *gémîné*. Il croit devoir le considérer comme un parasite particulier qui se développerait dans les cylindres épithéliaux des glandes de Lieberkühn et dans ceux des conduits biliaires. Il cite Hake et Nasse comme ayant trouvé des formes semblables, par masses, dans le foie du lapin. Kölliker a observé la même chose. Selon lui, les corpuscules du foie du lapin seraient des oeufs de bothriocéphale; ceux des villosités du même animal, plus petits que les premiers, des oeufs d'entozoaires, siégeant dans l'intérieur des villosités et peut-être aussi dans les cellules épithéliales distendues. Dans ce

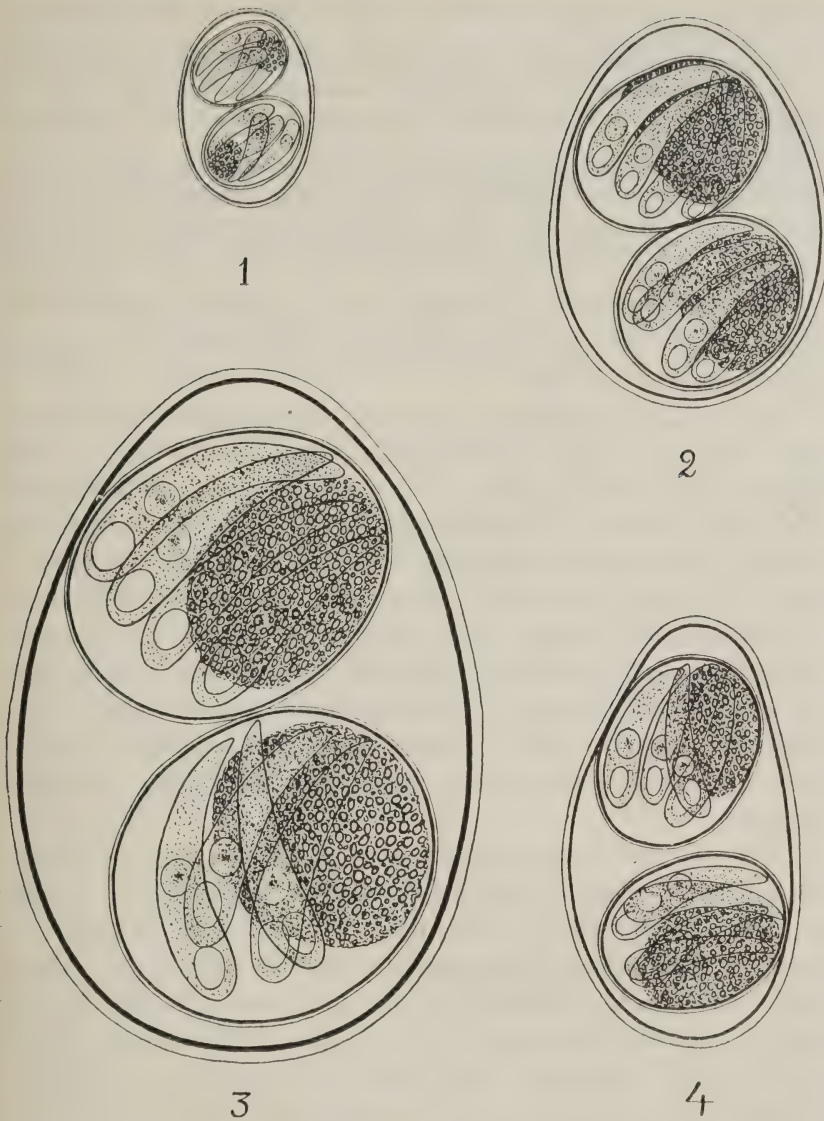


FIG. 1. Diagram of the oocysts of the *Isospora* of cats, dogs and men. $\times 2000$.

1. Oocyst of the small form which occurs in the deeper tissues of the villi of cats and dogs and man (*Isospora bigemina* and *Isospora hominis*).
2. Oocyst of the intermediate sized form which occurs in the epithelium of the villi of cats and dogs (*Isospora rivolta*).
3. Oocyst of the large form which occurs in the epithelium of the villi of cats and dogs (*Isospora felis*).
4. Oocyst of the large form which probably occurs in the epithelium of the villi of man (*Isospora belli*).

dernier cas, ils ressemblent, selon lui, à des grosses gouttes graisseuses remplissant les cellules épithéliales.

"Nous n'avons rien trouvé de pareil dans les cellules épithéliales de notre chat ; mais son foie renfermait des amas d'entozoaires plats, elliptiques, long d'un millimètre, probablement des douves. Ils étaient contenus dans des espèces de kystes.

"Quant à nous, tenant compte de l'énorme quantité des corpuscules en question, de l'absence de toute forme semblable dans la cavité de l'intestin, de leur absence dans toutes les villosités n'ayant point subi l'espèce de macération caractérisant les villosités farcies de globules graisseux, enfin de certaines formes de transition entre ces derniers et les *globules géminés*, nous croyons ne pas trop nous hasarder en rattachant les corpuscules en question au fait du mécanisme de l'absorption graisseuse. C'est tout ce que nous pouvons en dire quant à présent."

(Henri Finck : *Sur la physiologie de l'épithélium intestinal*. Thèse de Strasbourg, 1854, 2^e série, n^o 324, p. 17).

The important points to note from the above description are these. The sporocysts or *corpuscules géminés*, as Finck styled them, occurred in the substance of the villi and not in the epithelium of the cat's intestine. They measured 8 by 7 microns up to 10 by 9 microns, had definite contours, and were sometimes enclosed in pairs in a common membrane which was evidently the oocyst wall. As pointed out by Railliet and Lucet (1891), Finck's measurements have been wrongly quoted as ten times higher than they actually were by several observers, as, for instance, Pfeiffer (1890, 1891), Neumann (1892, p. 467). Dobell (1919) inadvertently refers to Finck's investigations as having been made on the dog, instead of the cat.

The reference to the similar but larger bodies seen by Remak, referred to by Finck, have to do with a paper by this author published in 1845 on the occurrence of what were evidently the oocysts of a coccidium in the intestinal wall of the rabbit. Vulpian (1858) cites Finck's observations, but it is not quite clear that he actually observed the oocysts of the cat coccidium himself. Rivolta (1873, p. 382), referring to the presence of psorosperms in domestic animals, says that they had previously been observed by Finck (1854), and also by Ercolani in 1859, in the cat. Perroncito (1882) also quotes Ercolani as having made this observation. Virchow (1860, p. 342 and p. 527) was the next observer to give any details of their structure, though, like Finck, he regarded them as products of fat absorption. He noted that the villi of the greater part of the intestine of a dog were infiltrated with psorosperms. They were on the surface of the intestine, but a larger number were free in the

intestinal contents. They occurred in the interior of the villi and were relatively small and regularly arranged in pairs enclosed by a double contoured membrane. He says they were evidently similar to the paired bodies described by Finck from the cat. He records and figures the oocysts of a coccidium which he found in the kidney of a bat, and which he regarded as similar to the one seen by him in the dog. The parasite of the bat evidently belongs to the genus *Isospora*.

Leuckart (1860, p. 11, and 1866, p. 21) mentions the fact that the intestinal mucosa of a dog which had been used for experiments with *Trichina* was much altered, and covered with a layer of small, egg-shaped psorosperms. He gives no details of their size or structure. He again (1863) refers to them, but is inclined to regard them as metamorphosis products in the intestinal wall. Another reference to these bodies found in another dog by the same author (1879, p. 282) gives no further information, but he was aware of Finck's work and evidently regarded the structures he had encountered as the same as those seen by Finck. He now describes the condition as due to an accumulation of parasites in the villi.

Rivolta (1874) gave a description of certain oviform cells (*cellule oviformi*) which he had found in the intestinal villi of dogs and cats. In his account, which deals entirely with those seen in dogs, he says they had walls showing a double contour, and varied in length from 8 to 12 or even 15 microns; while in breadth they measured 8 microns. The contents of some of the oviform cells are described as being granular and in the form of a nucleus, or as an elongated body like an embryo with granular material at its centre. In some, however, it is stated that in addition to a granular nucleus there were distinctly three or four elongated corpuscles somewhat irregular in shape. There are four figures accompanying this description, and two of these show quite clearly the granular mass and four small ovoid bodies. The oviform cells are described as occurring in the tissues of the villi especially near their tips and not in the epithelium. As evidence of this, a case is quoted where they were present in the villi of a dead animal which, owing to cadaveric changes, had lost its intestinal epithelium entirely. These oviform cells are again described by Rivolta (1877). In this paper mention is made of Finck's observations, and it is pointed out that invasion

by the cells produces grave alterations in the structure of the villi. In a further communication, Rivolta (1877a) states that he has found other cases of the infection in dogs. Examination of the oviform cells in Müller's solution showed that they constantly contained four long corpuscles with rounded ends. Two other stages are described and figured showing the bodies filled with a granular mass which may have indications of a central constriction. He ventures the suggestion that proliferation into two is taking place. The figures show this clearly. The length of the bodies is given as 13 to 16 microns, and the breadth as 12 microns. The statement is made that they are identical with the *corpuscules géminés* observed by Finck. Rivolta compares them with the psorosperms of the liver of the rabbit, and points out that they differ from these psorosperms in that they do not occur in the epithelium, and that segmentation takes place in the body of the host. He sums up his description by stating that there occur two types of these oviform cells. In one type the contents consist of a nucleus with four elongate corpuscles, while in the other there is a large granular nucleus which at times is in process of segmentation. In a later paper, Rivolta (1878) attempts to classify the psorosperms and gregarines of animals. He names the oviform cells of the dog and cat *Cytospermium villorum intestinalium canis*. He again states that two types of this parasite occur. The first varied in length from 8 to 12 microns, and had a breadth of 8 microns. Within was a single elongate granular body like an embryo. After a few days in water there developed three corpuscles and a granular nucleus. The second type was larger, and varied in length from 12 to 16 microns, and had a breadth of about 12 microns. The contents consisted of a single large granular mass which sometimes showed signs of segmentation.

From the above summary of Rivolta's descriptions it is clear that the larger type is the oocyst and the smaller one the sporocyst. He correctly observed the division of the granular mass into two sporoblasts, but did not realise that each of these gave rise to one of the smaller types which are sporocysts. It is evident that the wall of the oocyst was not very resistant, and easily liberated the sporocysts. In his earlier papers he correctly noted and figured the four sporozoites and the residual body within the sporocysts. It

is evident that the infection was limited to the internal tissues of the villi, and did not occur in the epithelium. The size of the oocyst was 12 to 16 microns by 12 microns, and that of the sporocyst 8 to 12 microns by 8 microns. The development was often completed before the oocysts had left the tissues. Incompletely developed sporocysts continued their development in water.

In his book, already noted above, Leuckart (1879, p. 282) discusses the changes produced in the intestinal wall by coccidia generally. He says he has seen these parasites in both dogs and cats. In the latter animals he states that they occur in the epithelium, where complete development takes place. In the case of the dog, they were in the villi, and he evidently regarded them as similar to the structures seen in this situation by Finck, but is doubtful about those described by Rivolta. As regards the cat, Leuckart is the only observer to refer to the complete development of the oocyst in the epithelium. Finck and Rivolta, together with Railliet and Lucet and Stiles, whose observations are considered below, all state that this takes place in the deeper tissues of the villi. Leuckart's account is not always clear as to the actual animal he is referring to, but the statement quoted definitely refers to the cat. As will be explained below, the oocysts of coccidia which develop in the epithelium do not commence to develop till they have left the body, so that Leuckart's statement is difficult to understand. It is possible that oocysts of the larger forms in the epithelium might develop in animals which had been dead for some considerable time, or that Leuckart actually observed the oocysts of the small form in an unusual situation in the epithelium. On the other hand, he may have seen both a large and a small form in these animals, and confused the two. It seems impossible to be certain of the form he refers to in the cat, but his statements about the one in the dog are much more precise.

The next observer to make a contribution to the subject from personal observations was Grassi (1879), who gives a brief account of a coccidium which he calls *Coccidium Rivolta*, from the intestine of the cat. The oocyst is described as giving rise to two spores, each of which contains four germs. In later papers (1882, 1883) he gives under the same name a more detailed description. The oocyst is said to be elliptical in shape with one end more pointed

than the other. At the pointed end there could be detected a sort of spiracle or micropyle. The measurements of the oocyst are given as 30·8 to 27 microns by 24 to 22 microns. Within it is a sphere varying in diameter from 10 to 20 microns, with a central clear area or nucleus. The sphere divides into two daughter spheres, each having a diameter of 14·3 microns. Two sporocysts result, within which are found four embryos and a large residual body. It is important to note that the parasite is described as occurring in the epithelium of the intestine. The description is accompanied by figures which illustrate clearly the structure of the oocysts. From Grassi's account there can be no doubt that he was dealing with a coccidium which was entirely distinct from that described by Finck, Virchow and Rivolta. As pointed out above, this distinction was recognised by Perroncito (1882) and others.

Pachinger (1887) states that he had seen a sporozoon in the oesophagus, stomach and whole length of the intestine of the domestic cat, and that he had encountered a similar form in the kidney of the dog. He says that it belonged to the monospore coccidia with four sickle-shaped bodies. It is probable he was observing the sporocysts of an *Isospora* of the cat, but there are no means of identifying it with certainty, as no measurements were given. The structures he records from the kidney of the dog are quite unidentifiable.

Railliet and Lucet (1888) published an account of oviform bodies which they found in the villi of a dog. They noted their occurrence in pairs, and remarked on their resemblance to the bodies described by Virchow and Rivolta. On account of their association in pairs, they hesitated to pronounce an opinion as to their coccidial nature. After further study, Railliet and Lucet (1890) gave a brief but clear description of these bodies as coccidia which they had observed in the pole cat as well as the dog. In the dog the oocysts are said to vary in length from 12 to 15 microns, and in breadth from 7 to 9 microns. The contents of each divide into two masses, and each of these gives rise to four spores. The fully developed oocysts may occur in the fresh villi, but usually complete development does not take place till they have been in water for a few days. The similar form with oocyst, measuring 8 to 12 microns by 6 to 8 microns, discovered in the pole cat (*Mustela putorius*) occurs in the deeper tissues of the villus.

Stiles (1891) refers to the work of Railliet and Lucet, and says that he has seen the cysts in the villi of dogs. He noted that each might contain a single large mass of cytoplasm or two separate masses suggesting a division into two of the large mass. Stiles gives the name *Coccidium bigeminum* to this parasite. Railliet and Lucet (1891), in a further communication on the subject, accept the name *Coccidium bigeminum* given by Stiles. They refer to the work of Rivolta and Finck, and say there is no doubt that these observers had studied the same organism. They now describe three varieties of the parasite as occurring in the dog, cat and pole cat, which they regard as varieties of *Coccidium bigeminum* owing to differences in the size of the oocysts:—

Coccidium bigeminum var. *canis* 12—15 × 7—9 microns.

Coccidium bigeminum var. *cati* 8—10 × 7—9 „

Coccidium bigeminum var. *putori* 8—12 × 6—8 „

As pointed out by Wasielewski (1904) these variations in size are insufficient to justify a separation of varieties on this basis alone.

The papers by Railliet and Lucet are not illustrated, but a figure by Railliet appears in the English translation of Neumann's work on 'Animal Parasites' (1892, p. 437). This figure again appears in the second edition of the *Traité de Zoologie Médicale et Agricole* by Railliet (1895, p. 145). Stiles (1892) gave a fuller and illustrated account of the *Coccidium bigeminum* of the dog. He described the development of the oocyst with the production of two sporoblasts and two sporocysts, and the formation within each sporocyst of four sporozoites and a residual body. A figure of a section of the villus shows the presence of oocysts containing the sporoblasts or undeveloped sporocysts within the deep tissues of the villus. The size of the oocyst is given as 14 by 8 microns.

From the description of Railliet and Lucet, and Stiles, it is evident that they were dealing with the coccidium seen by Finck, Virchow and Rivolta in dogs and cats. These observations appear to be the last ones which have been made on the small *Isospora* of these animals.

Wasielewski (1904) gave a detailed account illustrated with excellent microphotographs of the oocysts of a coccidium, called by him *Diplospora bigemina*, which he had observed in cats that were used for experiments on amoebic dysentery by Jürgens. The oocysts which he observed varied in size, and he gives a series of

measurements in microns as follows:—22 by 19, 25 by 20, 25 by 22, 35 by 23, 35 by 25, 35 by 27, 38 by 32, 40 by 28. He describes the development of the oocyst in detail. The contents contract to form a sphere, which has a diameter of 18 to 25 microns according to the size of the cyst. Two daughter spheres are formed by division of the large sphere, and these vary in diameter from 16 to 18 microns in the larger oocysts and from 11 to 12 microns in the smaller ones. The daughter spheres become sporocysts, within each of which are developed four sporozoites 11 to 12 microns in length and a residual body 6 to 8 microns in diameter. The earlier stages of the parasite were found only in the epithelium of the small intestine and never in the submucosa, so that Wasielewski considered that the statements which had been made of a coccidium limited to the submucosa required some qualification. Schizonts in the epithelium and motile merozoites free in the lumen of the intestine were also seen.

This coccidium is clearly distinct from that studied by Finck, Virchow, Rivolta, Railliet and Lucet, and Stiles. From the size of the oocysts they appear to fall into two categories, as noted by Reichenow (1921), the one with oocysts measuring 22-25 by 19-22 microns and the other with oocysts measuring 35-40 by 23-32 microns. Those of the first category clearly correspond with the parasite described by Grassi (1879, 1882, 1883). Wasielewski also gave measurements of 18 by 25 microns for the oocysts and 11 by 15 microns for the sporocysts of a form seen by him in the dog. He regarded it as *Coccidium bigeminum*, but it corresponds exactly with Grassi's *Coccidium Rivolta*.

Basset (1909) without giving any description of the parasites, discusses the pathogenic effect of coccidia, which he calls *Diplospora bigemina*, in young dogs. He also records a round coccidium, 14 microns in diameter, as occurring in dogs and ferrets, but there is no evidence that these were actually coccidia, as no mention is made of any development.

Swellengrebel (1914) gave a complete account of the development of a coccidium of the cat under the name *Isospora bigemina*, which appears to be identical with the large form noted by Wasielewski. He described for the first time the process of schizogony in the epithelial cells of the small intestine, the evolution of the macrogametocytes and microgametocytes, and formation and

development of the oocysts. The measurements of the oocyst are given as 39 to 47 microns by 26 to 37 microns. The sporocysts vary in length from 21 to 24 microns, and in breadth from 18 to 19 microns. Within the sporocyst there are formed four sporozoites measuring 18 by 4 microns, and a large residual body. Swellengrebel clearly states that the appearances are absolutely unlike those figured by Stiles, but hesitates to establish a new species.

Weidman (1915) described a coccidium, which he called *Coccidium bigeminum*, in 'swift foxes' in the Western United States. The oocysts varied from 25 to 40 microns in length by 25 to 30 microns in breadth. The sporocysts measured 16 to 20 by 14 to 18 microns. Owing to the difference in dimensions from the form described by Railliet and Lucet, and Stiles, Weidman suggests the 'new varietal name "*canivecolis*".' He gives figures of the oocyst containing two sporocysts, with four sporozoites and a residual body. Mesnil (1916) states that Weidman regarded it as a variety *canivecolis* of *Isospora bigemina*.

Wenyon and O'Connor (1917) found an *Isospora* of the cat very common in Alexandria, and Dobell (1919) records a similar experience in England in the case of cats used for experiments on amoebic dysentery. In both these instances the oocysts were of the large type. This was also the writer's experience during experiments on cats conducted in London in 1912.

Hall (1917) discovered a coccidium in dogs in Detroit. On account of its large size, he thought it was different from *Isospora bigemina*, but later Hall and Wigdor (1918) concluded that it was a larger form of the same parasite, and wrote of it as *Diplospora bigemina*. The oocysts measured 36 to 40 microns in length by 28 to 32 microns in breadth. The sporocysts had a diameter of 10 to 20 microns, and the sporozoites measured 12 by 4 microns. Oocysts of these dimensions occurred in the majority of dogs, but in one animal a smaller strain was seen, the oocysts measuring 20 by 18 microns and the sporocysts 12 by 11 microns, with sporozoites 10 microns in length by 3 microns in breadth. They state that this distinction in the size was quite marked, and that it raises the question as to whether the small one should be regarded as a variety or species. They go on to say that it is possible that there are several species of *Diplospora* in the dog

characterised by considerable difference in size. The length of time required for the development of the oocyst of the larger form was two days when kept in 10 per cent. potassium bichromate solution. Under other conditions, which they state more nearly resemble those of nature, the time required may be two weeks or longer.

Reichenow (1921), referring to the *Isospora* of cats and dogs, expresses it as his opinion that Wasielewski was probably dealing with a mixed infection of two distinct coccidia in the cats he examined. He also states that the form he had observed in the dog in Germany differs from that in the cat, and resembles the one with smaller oocysts studied by Wasielewski. For the oocysts of the dog form he gives a length of 21 to 24 microns, and a breadth of 18 to 20 microns. The sporocysts, which are oval in outline, measure 14 to 16 microns by 9 to 10 microns. Nöller (1921), in a brief reference to the coccidium of dogs and cats, refers to the large and small form in cats and the one in dogs. He has been able to infect young dogs in series with the oocysts. No details of the dimensions are given. Marotel (1922) studied the *Isospora* of the cat. His measurements are as follows:—

Oocysts $45-48 \times 34-36$ microns.

Sporocysts $22-24 \times 17-19$ microns.

Sporozoites $18-20 \times 4-5$ microns, residual body in sporocyst
10–12 microns.

He proposes to call the coccidium *Isospora cati*. In order to facilitate the following discussion, the various dimensions in microns given by the above observers for the oocysts and sporocysts of the dog and cat parasites are arranged in tabular form:—

TABLE I.

						Oocyst	Sporocyst
Finck (cat)	$8-10 \times 7-9$
Virchow (dog)	Like those described by Finck	...
Rivolta (dog and cat)	$12-16 \times 12$	$8-12 \times 8$
Grassi (cat)	$27-30.8 \times 22-24$	14.3
Railliet and Lucet (dog)	$12-15 \times 7-9$...
— (cat)	$8-10 \times 7-9$...
— (pole cat)	$8-12 \times 6-8$...
Stiles (dog)	$13.6-15.9 \times 7.9-9.9$...
Wasielewski (cat)	$35-40 \times 23-32$	16–18
— (cat)	$22-25 \times 19-22$	10–12
— (dog)	18×25	11–15
Swellengrebel (cat)	$39-47 \times 26-37$	$21-24 \times 18-19$
Hall and Wigdor (dog)	$36-40 \times 28-32$	10–20
— (dog)	20×18	12 × 11
Reichenow (dog)	$21-24 \times 18-20$	$14-16 \times 9-10$
Marotel (cat)	$45-48 \times 34-36$	$22-24 \times 17-19$

From the above table it will readily be seen that the oocysts described fall into three groups.

(1) There are the small forms described by Finck, Rivolta, Railliet and Lucet, and Stiles. Finck did not state the actual measurements of the oocysts, but from the size given for the sporocysts and the fact that in his description he says that two of these sometimes occur together enclosed by a common membrane, it is safe to assume that the oocyst would have dimensions similar to those described by Rivolta, Railliet and Lucet, and Stiles. The forms seen by Virchow are evidently similar, for he says they occur in the interior of the villi of dogs, are relatively small and regularly arranged in pairs enclosed by a thick, double contoured membrane. It is probable also that those described by Leuckart are of the same type.

(2) The second type has an oocyst of intermediate size. This was first seen by Grassi in the cat, later by Wasielewski in the cat and dog, by Hall and Wigdor in the dog, by Reichenow in the same animal, and possibly by Nöller in the cat and dog.

(3) The third type has an oocyst of much larger size. This was first definitely described by Wasielewski and Swellengrebel in the cat, and was seen by Wenyon and O'Connor, Dobell, Hall and Wigdor, and Marotel.

That these three types represent distinct species seems clear from the above records, and from observations to be recorded in this paper. In a recent study of English cats, the oocysts which occurred in the faeces were uniformly of large size, while those which were found in dogs' faeces were of the intermediate type. In one instance only was an infection of the cat with the small type seen. In this case the large form occurred also and it was clearly evident that the small one was limited to the deeper tissues of the villus, while the large one developed in the epithelium. Furthermore, development of many of the small oocysts was completed in the tissues of the villi, while those of the large form did not take place for some days after it had left the body. That the oocysts of the smallest form sometimes escape in the faeces in the undeveloped condition is demonstrated by an observation which has just been made by Mr. Leslie Sheather, of the Royal Veterinary College, with whom the writer has discussed his investigations on coccidiosis of dogs and

cats. By a process of concentration employed for the detection of worms' eggs in faeces, Mr. Leslie Sheather discovered that one dog was infected with the small form and another with that of intermediate size. The small oocysts measured about 12 microns in longest diameter, and like those of intermediate size were in the undeveloped condition. They proceeded to development when kept outside the body.

NOMENCLATURE

As regards the nomenclature of these parasites, there appears to be no great difficulty, though the name *Coccidium bigeminum* Stiles, 1891, has been employed indiscriminately for all three forms. Apart from Rivolta's name *Cytospermium villorum intestinalium canis* which he proposed in 1878, Grassi's name *Coccidium Rivolta* (1879) is the first one to be given to any one of these Coccidia. As pointed out above, Grassi was dealing with the oocysts of intermediate size in the cat, and, assuming that this form is the same as that of corresponding size from the dog, his name has priority. The name of this coccidium is, therefore, *Isospora rivolta* (Grassi, 1879). For the small form in the dog and cat the correct name is *Isospora bigemina* (Stiles, 1891). This leaves the large form in the dog and cat still unnamed, for the name *Isospora cati* suggested by Marotel (1922) cannot stand, as Railliet and Lucet (1891) employed the name *Coccidium bigeminum* var. *cati* for the small form in the cat, which if recognised as a distinct species from that in the dog, would become *Isospora cati*. For the large species the name *Isospora felis* is suggested. There are thus to be distinguished in dog and cat three species of *Isospora*:—

Isospora bigemina (Stiles, 1891).

Isospora rivolta (Grassi, 1879).

Isospora felis n. sp.

It is assumed that these different parasites are able to infect both dogs and cats, but it is possible that each animal has its own species. This can only be determined by more detailed observation and cross-infection experiments with clean animals. Railliet and Lucet (1891) have stated that the small forms in the cat, dog and pole cat are varieties of *Isospora bigemina*, while Weidman (1915) has made a similar suggestion for the large coccidium described by him

in the fox. His name was not properly proposed, as he merely says he advances a new varietal name 'canivecolis.' Mesnil (1916), in a summary of Weidman's paper, writes the specific name *canivecolis*, while Hall and Wigdor (1918) give it in full *C. bigeminum canivecolis*. This parasite, which is certainly not a variety of *Isospora bigemina*, may be identical with *Isospora felis*, but on the other hand it may be distinct. In the latter case the name *Isospora canivecolis* would be correct.

There exists also in dogs in England an intestinal *Eimeria* as recorded by Brown and Stammers (1922). For this parasite the name *Eimeria canis* is proposed.

Though Grassi (1879) proposed the name *Coccidium Rivolta* for the parasite he found in the cat, this name has been modified by several observers, in spite of the fact that Grassi repeated the name in his later papers (1882, 1883). Dobell (1919) in discussing this question, says that it is his view that Grassi's name should be changed by putting '*rivolta*' in the genitive, in which case the name would be *Isospora rivoltæ*. He thinks that a form such as '*rivoltai*' is objectionable. There seems, however, to be no real reason why the name should be changed at all, and to keep it in the form proposed by Grassi is in accordance with Rules of Nomenclature. Both the changes discussed by Dobell have, however, been previously made. Thus in the English translation of Leuckart's work (1886) there appears a note on page 221 initialed by the author (R. L.) in which the name *Coccidium Rivoltæ*, Grassi is used for the first time. Railliet (1895, p. 146) uses the name *Coccidium bigeminum* Stiles, 1891, for the small coccidium of the cat, dog and pole cat, and the name *Coccidium* (?) *Rivoltai* Grassi, 1881, for the form of intermediate size seen by Grassi. Neveu-Lemaire (1912) employs the name *Eimeria Rivoltai* Grassi, 1881, for the latter form, while Brumpt (1922), in the latest edition of his *Précis de Parasitologie*, uses the name *Isospora Rivoltai* Grassi, for all these parasites.

Several observers, including Wasielewski (1904), Martin (1909), Guiart (1910) and Hall and Wigdor (1918), place these parasites in the genus *Diplospora*, which, however, is generally recognised as a synonym of *Isospora*.

For convenience of reference, the following list of names

which have been employed for the *Isospora* of cats and dogs is appended :—

- Finck (1854). Corpuscules géminés.
 Vulpian (1858). Corps oviformes.
 Ercolani (1859). ? (Quoted by Rivolta and Perroncito.)
 Virchow (1860). Psorospermien.
 Leuckart (1860). Psorospermien.
 Davaine (1860). Corpuscules géminés.
 Leuckart (1863). Psorospermien.
 Leuckart (1866). Psorospermien.
 Eimer (1870). Psorospermien.
 Zürn (1874). Psorospermien.
 Rivolta (1874). Cellule oviforme.
 Rivolta (1877). Cellule oviforme.
 Rivolta (1877). Cellule oviforme.
 Davaine (1877). Corpuscules géminés.
 Rivolta (1878). *Cytospermium villorum intestinalium canis*.
 Leuckart (1879). *Coccidium perforans*.
 Grassi (1879). *Coccidium Rivolta*.
 Grassi (1882). *Coccidium Rivolta*.
 Bütschli (1882). *Coccidium Rivolta* Grassi.
 Perroncito (1882).
 Coccidium Rivolta.
 Cytospermium villorum intestinalium canis.
 Braun (1883). *Coccidium perforans*.
 Grassi (1883). *Coccidium Rivolta*.
 Balbiani (1884). *Coccidium perforans*.
 Leuckart (1886). *Coccidium Rivoltæ*, Grassi.
 Railliet (1886). *Coccidium Rivolta* Grassi.
 Pachinger (1887). Sporozoon.
 Neumann (1888). *Coccidium perforans*.
 Railliet and Lucet (1888). Corps oviformes.
 Zürn (1889). *Coccidium oviforme* Leuck.
 Blanchard (1889). *Coccidium Rivolta* Grassi, 1881.
 Pfeiffer, L. (1890). Coccidien.
 Railliet and Lucet (1890). Coccidies.
 Stiles (1891). *Coccidium bigeminum*.
 Pfeiffer, L. (1891). Coccidien.
 Railliet and Lucet (1891). *Coccidium bigeminum* vars. *canis*, *cati*, *putori*.
 Stiles (1892). *Coccidium bigeminum* Stiles, 1891.
 Neumann (1892).
 Coccidium bigeminum.
 Coccidium perforans.
 Coccidium Rivolta Grassi.
 Mosler and Peiper (1894). Coccidien.
 Railliet (1895).
 Coccidium bigeminum Stiles, 1891.
 Coccidium(?) *Rivoltai* Grassi, 1881.
 Braun (1895). *Coccidium bigeminum* Stiles 1891.
 Moniez (1896). *Coccidium bigeminum* Stiles (1891).
 Blanchard (1896). *Coccidium bigeminum* Wardell Stiles, 1891.
 Labbé (1896). *Coccidium bigeminum* Stiles.
 Wasielewski (1896).
 Coccidium bigeminum Stiles.
 Coccidium spec. inc. Rivolta Grassi.
 Labbé (1899). *Coccidium bigeminum* Stiles.
 Blanchard (1900). *Coccidium bigeminum* Wardell Stiles, 1891.
 Neveu-Lemaire (1901). *Coccidium bigeminum* Wardell Stiles, 1891.
 Doflein (1901). *Coccidium bigeminum* Stiles.
 Perroncito (1901).
 Coccidium bigeminum Wardell Stiles, 1891.
 Coccidium Rivolta.
 Neveu-Lemaire (1902). *Coccidium bigeminum* Wardell Stiles, 1891.
 Neveu-Lemaire (1903). *Coccidium bigeminum* Wardell Stiles, 1891.
 Braun (1903). *Coccidium bigeminum* Stiles, 1891.
 Minchin (1903). *Coccidium bigeminum* vars. *canis*, *cati*, *putori* Railliet et Lucet.
 Wasielewski (1904). *Diplospora bigemina*.
 Neumann (1905).
 Coccidium bigeminum.
 C. Rivoltæ (Grassi).
 Guiart and Grimbert (1906). *Coccidium bigeminum* Stiles.
 Lühe (1906). *Isospora bigemina* (Stiles).
 Braun (1906). *Coccidium bigeminum* Stiles, 1891.

- Neveu-Lemaire (1906). *Coccidium bigeminum* Wardel Stiles, 1891.
 Braun (1908). *Isospora bigemina* (Stiles) 1891.
 Neveu-Lemaire (1908). *Coccidium bigeminum* Wardel Stiles, 1891.
 Basset (1909). *Diplospora bigemina*.
 Guiart and Grimbert (1908). *Coccidium bigeminum* Stiles.
 Braun and Lühe (1909). *Isospora bigemina* (Stiles).
 Martin (1909). *Diplospora bigemina* Stiles.
 Doflein (1909). *Isospora bigemina* (Stiles).
 Braun and Lühe (1910). *Isospora bigemina* (Stiles).
 Brumpt (1910). *Coccidium bigeminum* Wardel Stiles, 1891.
 Guiart (1910). *Diplospora bigemina*.
 Doflein (1911). *Isospora bigemina* (Stiles).
 Fiebiger (1912). *Isospora bigemina* Stiles.
 ✓ Neveu-Lemaire (1912). *Eimeria Rivoltai* Grassi, 1881.
 Jollos (1913). *Isospora bigemina*.
 Brumpt (1913). *Coccidium bigeminum* (Wardel Stiles, 1891).
 Swellengrebel (1914). *Isospora bigemina* (Stiles).
 Braun and Seifert (1915). *Isospora bigemina* (Stiles) 1891.
 Doflein (1916). *Isospora bigemina* (Stiles).
 Fantham (1916). *Isospora bigemina*, Stiles, 1891.
 Wenyon and O'Connor (1917). *Isospora* of cats.
 Hall and Wigdor (1918). *Diplospora bigemina*.
 Dobell (1919).
 Isospora bigemina Stiles.
 Isospora rivoltai Grassi (1879).
 Reichenow (1921). *Isospora bigemina* (Stiles).
 Dobell and O'Connor (1921). *Isospora rivoltai* Grassi.
 Nöller (1921). *Isospora bigemina*.
 Mayer (1922). *Coccidien* ?
 Brumpt (1922). *Isospora Rivoltai* Grassi.
 Marotel (1922). *Isospora cati*.

DESCRIPTION OF THE COCCIDIA OF CATS AND DOGS

During the course of certain observations on the faeces of dogs, the results of which have been published by Brown and Stammers (1922), it became evident that dogs were sometimes infected with a species of *Eimeria* in addition to the commonly recognised *Isospora*. The oocysts of the latter parasite agreed, as regards dimensions, with those given by Grassi (1879, 1882, 1883) for the *Isospora* of the cat, by Wasielewski (1904) for the *Isospora* of the dog and small form in the cat, and by Reichenow (1921) for one in the dog, and were constantly smaller than the oocysts of the *Isospora* of the cat which was under observation at the same time, so that it seems highly probable that the common *Isospora* of dogs and cats belong to two distinct species. The oocysts of the *Eimeria* of the dog varied considerably in size, some of them being as large as those of the large *Isospora* found in the cats, while others were smaller even than those of the *Isospora* seen in the dogs. They differed in appearance from the oocysts of the *Isospora* of the same animal and showed a

much greater range in size, but it was only after material had been kept till development of the oocyst had completed itself that it was definitely recognised as an *Eimeria*. It is possible that this *Eimeria* has been seen before and regarded as an *Isospora*, but of this there is no evidence.

In the case of the *Isospora* of the cat the oocysts examined by the writer have been constantly of large size, except in one instance when very much smaller ones were also present. It was found by examination of the small intestine of this cat that the large oocysts were derived from an *Isospora* (*Isospora felis*) which was undergoing development in the epithelium of the intestinal villi, while the very much smaller ones belonged to another *Isospora* (*Isospora bigemina*) which was parasitic only in the deeper tissues of the villi. Furthermore, the oocysts of the latter form completed their development in the tissues, whereas those of the large form in the epithelium were in the usual undeveloped condition. The faeces of this cat had been examined on several occasions in connection with experiments with *Entamoeba histolytica*, but the only oocysts noted in the faeces were the large undeveloped ones of *Isospora felis*. The oocysts of *Isospora bigemina* were not seen in the faeces, and if they had been present to any extent they could not have escaped recognition. They were first detected when a scraping of the wall of the small intestine was made with a view to finding amoebae which had been seen in this situation in another cat with amoebic dysentery. It seems clear that the oocysts of the small form do not escape into the faeces so regularly as do those of the large one which develops in the epithelium. There is no doubt that there were two distinct species of *Isospora* in this cat.

A detailed study of the development of *Isospora felis* and *Isospora bigemina* as they occurred in the tissues of cats was undertaken, but *Isospora rivolta* of the dog was only investigated in the oocyst stages which occurred in the faeces.

***ISOSPORA FELIS* n. sp.**

The only complete account of the development of this common coccidium of the cat is that of Swellengrebel (1914), though Wasielewski (1904) had described the development of the oocyst and had seen other stages in the epithelium. In its main outlines

Swellengrebel's description is correct, but the growth of the microgametocyte was not fully traced. The supposed parthenogenesis of the macrogametocyte is capable of another interpretation, while the account of the changes undergone by the nuclei requires revision. It seems, therefore, desirable to redescribe the life-history as it has been studied in sections of the epithelium of the small intestine of cats.

Schizont. The smallest forms which can be found in the epithelial cells are only 5 microns in length (Plate IX, fig. 1). These are curved and somewhat sickle-shaped bodies which are pointed anteriorly and rounded posteriorly. They lie in vacuoles in the cells, and are attached to the cytoplasm of the cell by the pointed extremity. The nucleus is spherical and has a definite membrane. Within the nucleus is a body which, in staining reactions, does not appear to be rich in chromatin. It is usually applied to the nuclear membrane. In addition the nucleus contains a granular material which is probably chromatic in nature. Whether the large body should be regarded as a karyosome depends on the definition of this term. It does not stain intensely with Mayer's haemalum, has the appearance of plastin material rather than chromatin, and in this respect resembles a nucleolus rather than a karyosome. Growth of the parasite takes place till it has a length of about 10 microns and a diameter at its thickest part of about 5 microns (Pl. IX, figs. 2 and 3). Though plumper than the youngest forms, it still retains its elongate gregariniform character. While still in this condition nuclear division commences (Pl. IX, fig. 4) by division of the karyosome. The daughter karyosomes take up positions at the end of the now elongated nuclear membrane as two polar caps while a definite equatorial plate of small chromosomes is formed (Pl. IX, fig. 5). Two daughter plates are formed and the first nuclear division is completed by division of the membrane (Pl. IX, figs. 6-8). The two daughter nuclei have the same structure as that of the original nucleus. The second nuclear division takes place in a similar manner, as does also the third, though the karyosomes as a rule become smaller with each division (Pl. IX, figs. 9-12). When eight nuclei are present, the parasite has become more definitely ovoid in shape, and eight merozoites are formed by a budding process which leaves a definite residual body. Eight appears to

be the usual number for the merozoites, for the vast majority of schizonts which have been seen are of this type. The size of the merozoites, however, varies considerably even when only eight are present (Pl. IX, figs. 14 and 15). It seems possible that the small forms are destined to develop again into schizonts and the larger ones into gametocytes, but no definite proof of this could be obtained. Occasionally a smaller number of merozoites appeared to be formed (Pl. IX, fig. 16), but in such cases it is possible that the appearance was due to multiple infection of a cell by merozoites after schizogony had occurred, or to the fact that all the merozoites resulting from schizogony had not escaped from the cell. In several instances the occurrence of two merozoites in a single vacuole was undoubtedly due to two merozoites having invaded the same cell simultaneously. On the other hand, a large number of merozoites is sometimes formed, as pointed out by Swellengrebel (Pl. IX, figs. 17 and 18). In several instances as many as sixteen occurred, while a larger number was once seen. These forms, however, occurred rarely in the material examined, and, as stated above, the great majority of schizonts produced only eight merozoites.

It should be pointed out that the schizonts tend to stain very deeply, even with very dilute Mayer's haemalum, which proved to be the most satisfactory stain for these forms, so that unless thin sections are examined there may be considerable difficulty in making out the details of the nuclear divisions.

During growth the schizont is closely applied to the nucleus of the host cell, which becomes definitely altered in character.

Microgametocyte. The microgametocyte possibly commences as one of the larger merozoites (Pl. IX, fig. 19). Like the schizont, it retains, for a considerable period of its growth, its gregariniform character. When it has a length of about 12 microns (Pl. IX, fig. 20) the first nuclear division takes place. This is very similar in character to that of the schizont. The karyosome is present and divides in the same manner by dumb-bell constriction, while there is evidence that chromosomes are also formed (Pl. IX, figs. 20-22). Repeated nuclear divisions of the same type take place while the microgametocyte increases steadily in size. It finally loses its gregariniform character and becomes irregular in shape till it has a length of about 20 microns (Pl. IX, figs. 23-28). The increase in

bulk up to this stage has been relatively enormous. The details of the nuclear divisions are difficult to follow owing to the marked affinity the cytoplasm has for stains. This obscures details to such an extent that it is very difficult to detect the arrangement of the chromatin during the divisions of the nucleus.

After this a change takes place. The cytoplasm ceases to stain intensely, the chromatin material in the nucleus becomes much more definite and the karyosome decreases in size. Nuclear divisions continue, and these are definitely mitotic in character (Pl. X, figs. 1-3). The chromosome number has not been counted with accuracy, but it appears to be somewhere within the limits of 8 and 12. It appears that the nuclear membrane persists throughout nuclear division. The cytoplasm becomes fissured in various ways and loses still more its affinity for stains. Finally, when nuclear division is complete, the microgametocyte contains a large number of nuclei which have definite nuclear membranes within which are irregular masses of chromatin (Pl. X, fig. 4). The karyosome, which had decreased in size during the later divisions, is no longer clearly visible, but it seems probable that it is still present, for in the later divisions of the nucleus it is often possible to detect a small granule at each end of the mitotic figure. These two granules may be united by a fibre, so that the appearance of a minute karyosome dividing by elongation and constriction is produced. The nuclei then shrink, and become compact, deeply staining masses of chromatin (Pl. X, fig. 5).

Formation of microgametes commences by the outgrowth from the nucleus of a short process (Pl. X, fig. 6). The whole nucleus then elongates (Pl. X, fig. 7), and it seems probable that the short process represents the anterior end of the microgamete. The short curved masses then become more elongate, and fine tapering microgametes about 5 microns in length are formed (Pl. XI, fig. 1). The cytoplasm of the microgametocyte either collects into a single large residual body on the surface of which the microgametes lie, or it breaks up into several separate masses. A certain number of deeply staining granules remain in the residual body. The individual microgamete is pointed anteriorly and fine and tapering posteriorly. Sometimes there appeared to be a deeply staining granule near the anterior end of the microgamete. It is possible

that this granule functions as a blepharoblast from which the two flagella which Swellengrebel demonstrated arise. It seems probable that this granule is the karyosome or, as some would term it, the centriole which could be detected during the later divisions of the nuclei of the microgametocyte. When development of the microgametocyte is completed it may have a length of nearly 50 microns and measure over 30 microns in the two other diameters, so that it appears in many sections of a series. Well over two thousand microgametes may be formed by each microgametocyte. Swellengrebel was unable to trace the complete development of the microgametocyte, but it appears from his figures that some of the forms which he regarded as developmental stages of schizonts are really microgametocytes.

Macrogametocyte. It is assumed that the macrogametocyte commences as one of the larger merozoites (Pl. XI, fig. 2). At this early stage it has been impossible to differentiate between the young stages of either the microgametocytes, macrogametocytes or schizonts. The macrogametocyte can, however, be recognised at later stages owing to the fact that it has increased in size without nuclear division. It retains its gregariniform character, and is attached to the surface of the vacuole in the cell by its pointed extremity. The attachment is frequently on the nucleus, which in some cases is drawn into the vacuole (Pl. XI, figs. 3 and 4). On several occasions what appears to be a definite organ of attachment was seen (Pl. XI, fig. 5). Sometimes there is an appearance of a terminal sucker which has drawn into it a small pedicle of the cytoplasm of the cell. Even when the macrogametocyte reaches a large size the gregariniform shape is retained, so that the parasite may become doubled to accommodate itself to the space at its disposal (Pl. XI, figs. 6-8). During the stages of growth represented by Pl. XI, figs. 2-8 the cytoplasm stains deeply, with a tendency towards the accumulation of more intensely staining material round the nucleus in the later stages. The nucleus has increased considerably in size and possesses a large karyosome which has little affinity for stains. A change now takes place in the staining reactions. The deeply staining material round the nucleus increases in amount and there appears in the cytoplasm a number of deeply staining irregular bodies, while the cytoplasm itself becomes filled with vacuoles containing a clear refractile substance

(Pl. XI, fig. 9). The cytoplasm generally has less affinity for stains than it had previously, and it seems as if the substance which caused the cytoplasm to stain deeply in the earlier stages has now become aggregated in the irregular masses. The latter eventually disappear, leaving a clear cytoplasm filled with refractile globules (Pl. XI, figs. 10 and 11; Pl. XII, fig. 1). Finally the oocyst is secreted round the macrogametocyte. It does not become thick or resistant till it leaves the cell, for in fixed tissues the oocysts within the cells are permeable to fixatives and show no signs of the shrinkage and lack of proper fixation which is characteristic of those which are free in the lumen of the intestine.

During the growth of the macrogametocyte it is frequently noted that a granular substance accumulates in the vacuole between the parasite and the wall of the vacuole. This material, which often stains brilliantly with eosin, causes indentations in the macrogametocyte in various places (Pl. XI, fig. 11). Similar accumulations sometimes occur in the case of the microgametocytes (Pl. X, fig. 1).

Swellengrebel described a process of parthenogenesis of the macrogametocyte. Nothing comparable with this has been seen during the present investigations, and, judging from his figures, it seems that the stages he figures, in which definite nuclei are not present, are drawn from sections of macrogametocytes which did not include the nucleus but showed the deeply staining material which occurs around it (Text-fig. 2, p. 259). The large macrogametocytes naturally occur in several sections of a series, and the nucleus may only be found in one of these. In the sections on either side of this one the macrogametocytes will have the appearance of the forms figured by Swellengrebel as illustrating his process of parthenogenesis.

The foregoing description of the development of *Isospora felis* in the intestinal epithelium of the cat is of interest from several points of view. In the first place it is of importance to note that the parasite is limited to the epithelial cells. In no case has it been seen in the sub-epithelial tissues. The infection, moreover, appears to be confined almost entirely to the epithelium near the distal ends of the villi, there being little tendency for it to spread towards their bases.

During the growth of the young forms of the schizont and

gametocyte the parasite retains its gregariniform character to a relatively late stage. In this respect *Isospora felis* differs from many coccidia, which quickly assume the spherical form when growth commences. The fixation of the growing forms to the surfaces of the vacuoles by the pointed end and the development of what appears to be a definite organ of fixation still further increases the resemblance to certain gregarines, such as those of the genus *Lankesteria*.

The development of the microgametocyte merits special attention from the point of view of the behaviour of its nucleus. Schaudinn (1900), in his description of *Eimeria schubergi*, stated that the nucleus of the microgametocyte broke up into a chromidium, the granules of which collected in the form of a number of nuclei on the surface. A similar process was described by him (1902) for *Cyclospora caryolytica*, and again by Schaudinn and Siedlecki (1897) in the case of *Eimeria lacazei*. The majority of observers who have described the development of the microgametocytes of coccidia have followed Schaudinn in supposing that the numerous nuclei are formed from the chromidium into which the single nucleus breaks up. It was shown by Schellack (1912, 1913) and by Schellack and Reichenow (1913, 1915) for a number of coccidia, including the forms with which Schaudinn himself worked, that the latter's statements were incorrect, and that the nuclei of the mature microgametocyte resulted from repeated nuclear divisions from the original nucleus. A similar process had been described by Wasielewski (1904) for *Isospora lacazei* of birds, by Stevenson (1911) in the case of the *Eimeria* of the goat, by Léger and Duboscq (1910) for *Selenococcidium intermedium*, and by Siedlecki (1899) for *Adelea ovata*. It is very doubtful, therefore, if the microgamete nuclei are ever formed from chromidium, as Schaudinn maintained. It seems far more probable that in all coccidia they result from repeated nuclear divisions, as described above for *Isospora felis*.

The structure which has been called the karyosome is present in all the stages of schizogony and in the merozoites. It occurs during the early nuclear division stages of the microgametocyte, but in the later stages is represented by a minute granule. Whether this is to be regarded as a centrosome or centriole is a difficult question to decide. It certainly occupies the position in mitotic division that

a centrosome would occupy, and furthermore, it is probably this granule which occurs at the anterior end of the microgamete, and from it the flagella may originate. The karyosome is constantly present during the growth of the macrogametocyte, though it usually becomes smaller towards its maturity. Whether it disappears before fertilisation takes place has not been definitely determined, but it is certainly present during the nuclear division of the zygote and sporoblast. There was no indication that the karyosome was discharged from the nucleus prior to fertilisation. Though the latter process was not actually observed in stained preparations, in a few cases the nucleus of the fully grown macrogametocyte was elongated. It seems probable that this was an elongation preparatory to fertilisation, and if so it is worthy of note that the karyosome was still present in the nucleus.

Oocyst. As regards the oocysts themselves (Pl. XII, figs. 12-15) the measurements of a large number showed that they vary in length from 39 to 48 microns and in breadth from 26 to 37 microns, the majority measuring about 45 by 33 microns. These figures are practically identical with those given by Swellengrebel. Wasielewski, however, saw smaller forms in the cat, his measurements being 22 to 40 by 19 to 28. It seems possible that cats may be infected with both *Isospora felis* and *Isospora rivolta*, in which case Wasielewski's figures would cover a mixed infection with these two forms. Grassi appears to have been dealing with a pure infection of *Isospora rivolta* in the cat.

The development of the living oocyst of *Isospora felis* has been followed by Wasielewski, Swellengrebel and others, and there is little to add to their descriptions. Owing to the impermeable nature of the oocyst wall, it is difficult to obtain satisfactorily fixed preparations of the nuclei during its development. A certain number of preparations was, however, obtained in the following manner. Small quantities of the material containing oocysts in various stages of development were crushed between a slide and cover-glass in order to rupture the cysts, and films fixed in Schaudinn's fluid and stained with iron haematoxylin were made in the usual manner. There was thus obtained a number of stained preparations of the different stages.

The nucleus of the zygote (Pl. XII, fig. 2) has very much the

same appearance as that of the macrogametocytes in the tissues. A karyosome is still present, though it appears to be smaller. The same type of nucleus occurs in other stages, including those of the sporoblasts (Pl. XII, figs. 3-7), but in these the karyosome has increased relatively in size. A few nuclear divisions were seen, but these were not sufficiently numerous for many details to be made out. The stages which were seen resembled those which occur in the early stages of development of the microgametocyte, except that the karyosomes are smaller. The nuclei in various stages of development of the oocyst are depicted in Pl. XII, figs. 2-10.

The zygote nucleus (Pl. XII, fig. 2) is a spherical body consisting of a definite membrane, within which a number of fine granules and one larger mass—the karyosome—occur. Whether the karyosome is present in the earliest stage of the zygote nucleus could not be determined, as stained preparations of the fertilisation process were not seen. Satisfactory pictures of the first nuclear division were not observed, so that no statement can be made regarding a possible reduction in the number of the chromosomes. The two nuclei of the binucleate stage are shown at Pl. XII, fig. 3. Both nuclei are decolorized, and the small granule at the centre of the karyosome is well seen. The single nuclei of the two sporoblasts have the same structure. The first division in the sporoblast is shown at Pl. XII, fig. 4. The daughter karyosomes occupy the poles of the spindle, while daughter plates of chromosomes are also present. The nuclei of the binucleate stage of the sporoblast are shown at Pl. XII, fig. 5, and here again the nuclei are of the same type. The second nuclear division in the sporoblast shows two spindles with the karyosomes at the poles of the spindle, and definite equatorial plates (Pl. XII, fig. 6). The resulting four nuclei, with somewhat deeply stained karyosomes, are shown at Pl. XII, fig. 7.

Good preparations of sporozoites were fairly numerous. These measured from 10 to 15 microns in length (Pl. XII, figs. 8-11), being smaller after fixation than in the living condition. In some a large vacuole occurs near one end. This is evidently the position of the refractile body often seen in the living sporozoites (Pl. XII, fig. 15). The nucleus was spherical and contained a relatively large karyosome. In specimens from which the stain had been sufficiently extracted (Pl. XII, fig. 8) the karyosome was pale, and at its centre

was a small deeply staining granule. It thus appears that the karyosome is present in all stages of the nuclei during sporogony, though varying considerably in size.

The sporozoites appear to be budded off in pairs from the ends of the sporoblast. Two buds appear at each end, and these grow into elongate finger-like processes into which the nuclei enter. During their growth they turn over the surface of the residual body and lie between it and the wall of the sporocyst.

An important point to note is that the oocyst commences to form as a thin membrane while the macrogametocyte is still within the epithelium, but it does not become a resistant structure till the macrogametocyte has left the cell for the lumen of the intestine. In no case was there any indication that the further development of the contents took place, either in the cells or in the lumen of the intestine. Retraction of the zygote and division of the latter into two sporoblasts, which are the first steps in the development after the oocysts leave the body, were never noted in the case of oocysts within the epithelium or in the lumen of the intestine. It follows, therefore, that whenever observers have described the occurrence of paired bodies in the intestine wall they cannot have been referring to the oocysts of *Isospora felis*.

ISOSPORA BIGEMINA (STILES, 1901)

This coccidium was discovered in one cat which had been employed for experiments with *Entamoeba histolytica*. The cat died during the night, but at the autopsy next morning it was still warm and perfectly fresh and the amoebae active and in healthy condition. The cat had evidently been dead only a short time. It is important to note this fact, for many of the oocysts of *Isospora bigemina* which occurred in the submucosa were fully developed. It seems hardly possible that they could have completed their development in the short time following the death of the cat. This is all the more probable in view of the fact that oocysts of *Isospora felis* which were also present in the intestine were quite unchanged. It can safely be assumed, therefore, that the appearance of *Isospora felis* in the tissues and in the intestine were those which occurred during life. This accords with the descriptions which have been given by Finck, Virchow, Leuckart, Railliet and Lucet, and Stiles.

The sporocysts of this coccidium were first seen in scrapings of the wall of the small intestine after the death of the animal. It was at first thought that they were fully developed sporocysts of *Isospora felis*, but their small size was against this view. Further examination showed that they really occurred in pairs enclosed in an oocyst which was easily ruptured between the slide and cover-glass. The sporocysts had fairly thick, double-contoured walls, and contained four sporozoites and usually a residual body. The oocyst wall enclosing them was of a more delicate nature, and was closely wrapped round the two sporocysts. There was no indication of a micropyle in the oocyst.

Sections of the small intestine showed that the parasite did not occur in the epithelium, but was limited entirely to the sub-epithelial tissues of the villi, especially near their distal ends, some of which were swollen and packed with oocysts in various stages of development. The epithelium contained *Isospora felis*, which on account of its large size contrasted very markedly with the much smaller form in the tissues. Text-figure 2 is from a drawing of a transverse section of a villus, and shows two macrogametocytes, one with a nucleus and the other with the central granular mass to the side of the nucleus, a fully developed microgametocyte with microgametes, and a young micro- or macrogametocyte of *Isospora felis* in the epithelium, and six fully developed oocysts of *Isospora bigemina* in the sub-epithelial tissues.

The earliest stages of *Isospora bigemina* are seen as minute spherical bodies enclosed in vacuoles in the cytoplasm of mononuclear cells (Pl. XIII, fig. 1). Whether these are endothelial cells or not has not been determined. No endothelial cells which were evidently on the walls of blood vessels were found infected. These young forms are barely 2 microns in diameter. They grow into schizonts which are 5 to 6 microns in diameter, and produce about twelve merozoites. Owing to their small size, it is exceedingly difficult to follow the development in the sections (Pl. XIII, figs. 2-4). The microgametocytes have not been definitely identified, though several structures have been seen which are possibly of this nature. One of these has been drawn (Pl. XIII, fig. 5), and it would seem not improbable that the minute curved bodies are microgametes surrounding a residual mass of cytoplasm. The macrogametocyte

develops into an ovoid body 10 to 12 microns in length (Pl. XIII, figs. 6 and 7). It becomes enclosed in an oocyst (Plate XIII, fig. 8), within which it divides into two sporoblasts, which in their turn form sporocysts the walls of which are thicker than that of the oocyst. Within each sporocyst four sporozoites are produced (Pl. XIII, figs. 9-11). In many sporocysts it has been impossible to recognise



FIG. 2. Section of a villus of the cat showing *Isospora felis* in the epithelium and *Isospora bigemina* in the deeper tissues. In the epithelium are seen two macrogametocytes, one cut through the nucleus and one cut to the side of the nucleus: one microgametocyte which has given rise to numerous microgametes and a residual body, and one young form which may be a young macrogametocyte. In the interior of the villus are seen six mature oocysts of *Isospora bigemina*. $\times 1500$.

a residual body, but such a structure is definitely present in some cases. It appears that it breaks up and disintegrates after the sporozoites have been formed.

As regards the fate of the fully formed oocysts, there is no definite information to offer, except that they were not detected during the examination of the faeces made before death. In the sections of the intestine the epithelium was in many cases absent, so that escape

of the sporocysts would be an easy matter if such a change occurred in life. The heavily infected villi were considerably altered in appearance. They were swollen, and an excess of cells was present. It seems probable that such altered villi would break down during life and liberate the oocysts. These would not appear in the faeces regularly, as in the case of *Isospora felis* which develops in the epithelium, but would occur at intervals, whenever a villus broke down sufficiently to discharge its contents, which would include oocysts in various stages of development.

The question of a possible relationship between this parasite and the very much larger *Isospora felis* which develops only in the epithelium has been considered. It might be urged that if *Isospora felis* developed in the sub-epithelial tissues it might take on the character of the smaller form. The latter, however, has only been seen in one animal, while many infected with *Isospora felis* alone have been studied. It seems clear, therefore, that the small form is a distinct species.

The undeveloped oocysts of *Isospora bigemina* have recently been detected in the faeces of a dog by Mr. Leslie Sheather, as noted above.

ISOSPORA RIVOLTA (GRASSI, 1879)

This coccidium has only been studied in the oocyst stage as found in the faeces of three dogs. Mr. Leslie Sheather has also seen the oocysts in the faeces of a dog at the Royal Veterinary College. The oocyst has much the same shape as that of *Isospora felis*, but is smaller. The measurements obtained from the three dogs agree very closely with those given by Grassi (1879, 1882, 1883) for the form in the cat, and Reichenow (1921) for the one in the dog. The dimensions given by Wasielewski (1904) for the oocysts seen by him in the dog are very much the same, as also the smaller series found by him in the cat. Hall and Wigdor (1918) evidently met with this parasite in one dog. The reference made by Nöller (1921) to a large and small form in the cat may refer to *Isospora felis* and *Isospora rivolta*.

Four stages of development of the oocyst are shown at Pl. XIII, figs. 12-15. As seen in English dogs, they vary in length from 20 to 24 microns and in breadth from 15 to 20. Large oocysts

like those of the cat are never seen, though, as pointed out above, when the larger oocysts of *Eimeria canis* were present, it was at first thought that these belonged to *Isospora felis*. The difference in size between the oocysts of *Isospora felis* and *Isospora rivolta* was so constant that there can be little doubt that two species are represented, as Reichenow (1921) has suggested.

***EIMERIA CANIS* n. sp.**

The oocysts of this coccidium were seen in three dogs, as recorded by Brown and Stammers (1922). In two of them the infection was a small one, while in the other it was fairly heavy. The remarkable feature of the oocyst is its great range in size. In this respect it resembles *Eimeria deblickei* of the pig, the oocysts of which were described by Cauchemez (1921). Another feature which is of interest in the case of *Eimeria canis* is that the sporocysts show the same proportional variation in dimensions as do the oocysts. It is evidently incorrect to suppose that in coccidia the sporocysts remain fairly constant in size in spite of variations in the dimensions of the oocysts. The oocyst of *Eimeria canis* varies in length from 18 to 45 microns, and in breadth from 11 to 28 microns. The general shape of the oocyst will be appreciated from the figures (Pl. XIII, figs. 16-19, and Pl. XIV, figs. 1-8). The cyst wall constantly had a peculiar pink colour, and what seemed to be the true oocyst wall was enclosed by a somewhat irregular thick membrane which gradually peeled off during the development outside the body. When this membrane had separated, the colour of the cyst was still the same, though much paler. The course of the development is illustrated in the drawings. It will be noted that a definite micropyle could be detected in some oocysts (Pl. XIII, figs. 16 and 18, and Pl. XIV, fig. 1) and that the enclosed cytoplasm was sometimes attached to it by a strand (Pl. XIII, fig. 16). An inner membrane indicated by radiating lines could also be detected in some of the oocysts (Pl. XIII, figs. 18 and 19, and Pl. XIV, figs. 1 and 2). During the formation of the sporoblasts there was a striking resemblance to *Eimeria stiedae* of the rabbit, as described by Metzner (1903). Pyramidal elevations with clear hyaline apices were formed. The sporocysts had the characters shown in the

drawings (Pl. XIV, figs. 5-8). It will be noted that at the narrower end there is a definite elevation or knob. In many respects the oocysts resemble those of the coccidium of the rabbit. Since the paper by Lucet (1913) appeared, it has been assumed that there are two coccidia in the rabbit, the one, *Eimeria stiedae*, with larger oocysts than the other, *Eimeria perforans*, as first clearly stated by Leuckart (1879). The former, according to Reichenow (1921), who agrees with this view, occurs in both the liver and intestine. In some cases the liver alone is infected, in others only the intestine, while in other animals both are found to harbour the coccidium. The other form, *Eimeria perforans*, is apparently limited to the intestine, though information on this point is not very definite. There seems, however, no reason to suppose that the coccidium of the dog represents two species, though in many respects it corresponds with a mixed infection of two forms in the rabbit. The great variation in size of the oocysts of *Eimeria canis* raises the question as to whether there are actually two coccidia in the rabbit or only one.

It does not seem possible to identify the form in the dog with the common rabbit coccidium, though Bruce (1919) has described a coccidium of the rabbit in America the oocysts of which resemble those of *Eimeria canis* in the presence of the layer of material covering the wall, in its pinkish orange colour and the marked range in size. Bruce was inclined to regard this parasite as a new species, or a variety of the common rabbit coccidium. It certainly resembles *Eimeria canis* more than any other recorded coccidium.

It should be mentioned, however, that Guillebeau (1916) has described a still smaller coccidium, which he says occurs in the liver cells of dogs. He identified it with *Eimeria stiedae*, though the oocysts measured only 12 by 7 microns. As pointed out by Reichenow (1921), the situation of the parasite in the liver cells is a most unusual one for coccidia. The figures given by Guillebeau do not assist in arriving at a conclusion as to the nature of the organism. Chierici (1908), quoted by Martin (1909), recorded a coccidium which he found in the bile of a cat. The oocysts had a thick, double-contoured wall, were oval in shape, and measured 26 to 30 microns in length by 17 to 20 microns in breadth. Development with the formation of four sporocysts, each with two sporozoites,

occurred. It is evidently a coccidium of the genus *Eimeria*, but whether it is identical with *Eimeria canis* cannot be determined.

Virchow (1865, p. 356) records his discovery in the gall-bladder and bile ducts of one dog of numerous egg-shaped psorosperms with thick, double-contoured shells. No further description is given, so that it is not possible to form an opinion as to whether these were oocysts of coccidia or eggs of a trematode. Another reference to similar structures is by Rivolta (1878), who gives the name *Cytospermium hepatis canis familiaris* to certain oval bodies which Perroncito had found in the bile ducts of the dog and which he had called *cellule oviforme del fegato del cane*. Perroncito (1882, p. 98) refers to what are evidently these bodies as '*Citospermio del fegato del cane*.' He gives also the name '*Cellule oviforme del fegato del cane, Perroncito*.' They are described as measuring 48 to 52 microns in length by 21 to 32 microns in breadth. There is a capsule 2 microns in thickness, and at one pole an operculum. The contents divide into two to eight masses. There is little doubt that these bodies are eggs of a trematode. It appears that the first reference was made by Perroncito (1876), but this paper has not been consulted.

ISOSPORA OF MAN

The facts which have been explained above have a direct bearing on the status of the *Isospora* which has been recorded from human beings. It will be necessary to review the history of the discovery of the parasite. The first record of the occurrence of such a coccidium is that of Virchow (1860, p. 527), who mentions a case which was brought to his notice by Kjellberg. He found at post-mortem Psorosperms in the villi, which agreed entirely with those that he (Virchow) had seen in dogs ('*welche ganz mit denen übereinstimmen, die ich beim Hunde gesehen habe*'). The Psorosperms occurred in the interior of the villi, and especially towards their ends ('*in dem Innern und zwar gegen die Spitze der Darmzotten*'). Of the form seen by him in the dog, he says that in the interior of the villi he saw numerous Psorosperms of relatively small size regularly arranged in pairs with a double-contoured membrane ('*Indess habe ich neulich erwähnt (S. 342), dass ich in einem Hunde im Innern der Darmzotten sehr häufig Psorospermien*

antraß; es waren relativ kleine, regelmässig zu zweien aneinander-gesetzte mit starker, doppeltcontourirter Membran versehene Körper'). He goes on to state that they must have been like the forms seen by Finck in the cat. From Virchow's statements, the only conclusion justifiable is that he saw in man a small coccidium like *Isospora bigemina* of the cat and dog.

The next reference is that by Eimer (1870), but this is much less satisfactory than that of Virchow. Eimer says that he saw Psorosperms in two men who were examined post-mortem in Berlin. The intestinal canal was described as being filled and the epithelium completely infiltrated with Psorosperms. He says they were like those seen by him in mice and other animals. In both the human cases the epithelium of the greater part of the intestine is described as having been devoured by the Psorosperms, as occurs in infected mice. The contents of the Psorosperms were finely granular. Eimer furthermore states that he observed all stages of the division of the contents, but gives no clear account of the process. From these meagre details it appears impossible to identify the Psorosperms seen by Eimer. Whether they were coccidia at all is far from clear. They evidently did not show the same arrangement in pairs noted by Virchow, for such a striking appearance would hardly have escaped his notice. The only points in favour of the view that they were coccidia are the statements that they occurred in the epithelium, and that they resembled undoubted coccidia of the mouse and other animals. As coccidia belonging to both the genera *Isospora* and *Eimeria* occur in man, it is fruitless to speculate as to which genus the form seen by him belongs.

Rivolta (1873) describes certain corpuscles he found in the faeces of man, but there is no evidence whatever that these were oocysts of coccidia. Similarly, the bodies seen by Grassi (1879), and which he regarded as coccidia, were probably cysts of *Giardia*. Rivolta (1879) proposed the name *Cytospermium hominis* for the psorosperms found in man by Eimer. The name is given explicitly to Eimer's psorosperms, and Rivolta makes no mention of the bodies originally described by him in 1873. Thus Rivolta's name *Cytospermium hominis* was given to certain bodies seen by Eimer which may or may not be coccidia, and even if they were coccidia are quite unidentifiable.

Railliet and Lucet (1890) described the small coccidium of the villi of dogs. They recognise in these the form named *Cytospermium villorum intestinalium canis* by Rivolta (1878). They correctly followed the development with the production of two sporoblasts, each of which gave rise to a sporocyst containing four sporozoites. The oocysts measured 12 to 15 microns by 7 to 9 microns. They state that they had seen coccidia in the faeces of a woman and her child who were suffering from chronic diarrhoea. The coccidia were regularly ovoid, and some of them contained granular protoplasm, including a number of refringent globules. Others contained a large granular mass without globules. The average size was 15 by 10 microns. They recognise, however, that they differed in certain respects from the forms seen in the dog.

In a later paper, Railliet and Lucet (1891) accept the name *Coccidium bigeminum* given by Stiles (1891) to the small coccidium of the dog. As pointed out above, they recognised three varieties of this organism, *Coccidium bigeminum* vars. *canis*, *cati* and *putori* in the dog, cat and pole cat, respectively. They say that a fourth variety probably also exists, namely, *Coccidium bigeminum* var. *hominis*, the form which was seen by Kjellberg and described by Virchow (1860). They make no mention of the bodies described by themselves in 1890. Railliet (1895), however, ascribes to the species *Coccidium bigeminum* the often quoted parasite discovered by Kjellberg. As regards the bodies seen by Railliet and Lucet (1900) in two human cases, Railliet groups them with those described from man by Grassi and Rivolta as doubtful forms about which it is not possible to express an opinion. He states, however, that the size of those recorded by Railliet and Lucet (15 by 10 microns) brings them into relation with *C. bigeminum*. Six pages further on in his book, Railliet again asserts that the parasite discovered by Kjellberg must without doubt be placed in this species (*C. bigeminum*), as it was situated in the interior and towards the tips of the villi, and resembled the form seen by Virchow in the dog. It is thus evident that Railliet and Lucet, in employing the name *Coccidium bigeminum* var. *hominis*, were naming not the form seen by themselves, but Kjellberg's parasite recorded by Virchow (1860).

From what has been said above, it will be apparent that in only one of the records, namely that of Virchow, is it possible to make

an accurate deduction that a coccidium was being dealt with. Rivolta's name *Cytospermium hominis* refers to Eimer's parasite which cannot possibly be identified. If a coccidium at all, it may have been an *Isospora* or an *Eimeria*, but nothing more definite can be asserted. In the case recorded by Virchow, however, we know that he was familiar with the small *Isospora* of the dog. He recognised that the latter occurred in the tissues of the villi and not in the epithelium, and that it occurred in pairs and was like the parasite of the cat described by Finck. Of the human form, he says it occurred in the interior of the villi, especially towards their distal ends, and that it agreed entirely with the one he had seen in the dog. The only possible conclusion which can be drawn legitimately from these precise statements is that Virchow actually meant what he said and was observing in man a small *Isospora* like *Isospora bigemina* of dogs and cats. With the very doubtful exception of the bodies seen by Railliet and Lucet (1890) this small coccidium has not since been discovered. At first sight this may seem surprising, but there appears to be a possible explanation. When Finck made his observations on the cat he was concerned mostly with the changes undergone by the intestinal epithelium during digestion rather than with the faeces. He was actually examining the intestinal wall itself, and not the dejecta of his animals. Similarly, Virchow and Rivolta, who saw the small *Isospora* of dogs, were concerned mostly with the wall of the intestine, and the same appears to be true of Railliet and Lucet, and Stiles. As pointed out above, the presence of *Isospora bigemina* in the cat was only detected by the writer when scrapings were made from the intestinal wall. In these scrapings the thick-walled sporocysts, often arranged in pairs enclosed by a common membrane, were very striking objects, whereas the incompletely formed oocysts of the large *Isospora felis* which were also present were not nearly so easily seen, and might readily have been mistaken for enlarged tissue cells. If examination in this case had been limited to the faeces the small forms would have been missed entirely, and only the oocysts of the large form seen.

Grassi, however, was concerned largely with the examination of the intestinal contents and faeces, with the result that he discovered the oocysts of the intermediate sized *Isospora rivolta* in the cat.

When he examined the intestinal epithelium he noted that they were present in the epithelial cells, but there was no indication of a paired arrangement as in the case of the small *Isospora bigemina* seen by Finck and others. Since Grassi's time, Wasielewski and other observers, who have likewise studied the faeces, have noted in cats and dogs both *Isospora rivolta* and *Isospora felis*, but never the small *Isospora bigemina*. The developmental stages of the larger forms have been seen only in the epithelial cells, and never in the paired condition in the tissues of the villi. It is not improbable that the tissue-invading small form has been frequently missed owing to failure on the part of investigators to examine scrapings from the intestinal wall itself. Virchow discovered the small form in man because he adopted this method, and it is probable that it would have been re-discovered in recent years had this practice been continued and if examinations had not been limited to the faeces alone.

During the extensive examination of faeces of men necessitated by the exigencies of the war, the oocysts of an *Isospora* were discovered on many occasions. They were first seen by Woodcock (1915) and then by the writer (1915), who demonstrated their development and proved that they actually belonged to the genus *Isospora*, as had been suggested by Woodcock. In a recent paper, Connal (1922) has shown that over one hundred and fifty cases of infection with this parasite are on record. The oocysts measure from 25 to 30 microns in length by about 12 to 15 in breadth. They thus correspond in size with those of *Isospora rivolta* of cats and dogs. They differ, however, in shape, so that they cannot be identified with the parasite of dogs and cats. From what has been said above, it is evidently impossible to identify this human *Isospora* with the small form (*Isospora bigemina*) of cats and dogs or with the small form (*Isospora hominis*) seen by Virchow in man. The fact that the oocysts appear in the stool in the undeveloped condition is strongly suggestive of a development in the epithelium like *Isospora rivolta* and *Isospora felis* of cats and dogs.

Dobell (1919), in his careful review of the coccidia of man, based his arguments on the assumption that only one *Isospora* occurred in cats and dogs, and under the name *Isospora bigemina* he included the small, intermediate and large-sized forms of these animals.

Hence in his discussion of the name which should be applied to the *Isospora* of man, with every justification he included under the name *Isospora hominis* the small form described by Virchow and the much larger form discovered during the war. When it is realised that the small form in cats and dogs which develops in the tissues of the villi is distinct from the larger forms which develop in the epithelium, this position as regards the human parasites at once becomes untenable. The small *Isospora* of man described by Virchow was named *Isospora bigemina* var. *hominis* by Railliet and Lucet (1891), a name which becomes *Isospora hominis* Railliet and Lucet, 1891. As we have seen, the name *Cytospermium hominis* of Rivolta was given to unidentifiable structures seen by Eimer (1870). Dobell (1919) recognises this latter fact, but adopts the position that it is better to assume that Eimer was actually dealing with the form described by Virchow, and strongly urges that this view be accepted. But this statement was made on the assumption that the small forms in the dog and cat were identical with the larger ones, an attitude which is maintained by Dobell and O'Connor (1921), who employ the name *Isospora rivoltae*. It seems unwise to make this assumption, as there are absolutely no data to indicate the nature of the structures seen by Eimer. It is more logical to adopt the name *Isospora hominis* Railliet and Lucet, 1901, for the small *Isospora* of man, and to regard Rivolta's name *Cytospermium hominis* as a *nomen nudum*.

As regards the large *Isospora* of man, no special name has been given to it, though Savage and Young (1917) employed the term *Coccidium isospora* for this parasite. As pointed out by Dobell (1919), this is evidently a misprint or *lapsus calami*. The intention of the writers was not to introduce a new name, but to refer to a coccidium of the genus *Isospora* in contradistinction to one of the genus *Eimeria*, as coccidia belonging to both these genera had been recorded from man during the examinations for intestinal protozoa made during the war. If, however, it is claimed that the name was correctly presented, then, *Coccidium* being a synonym of *Eimeria*, Savage and Young's name becomes *Eimeria isospora*, and one would have to conclude that they were recording an *Eimeria* of man. There is actually no evidence in the paper that this was not the case, however improbable such a conclusion may be. Their name is, strictly speaking, a *nomen nudum*.

An appropriate name for the *Isospora* of man which figured so largely during investigations on the intestinal parasites of man conducted during the war would be *Isospora belli*. It may at first sight appear to cause confusion to introduce a new name for a parasite which is now generally known as *Isospora hominis*, but Virchow (1860) so definitely referred to a small *Isospora* of man, which was named *Coccidium bigeminum* var. *hominis* by Railliet and Lucet (1891), that to submerge this form by applying the name to a much larger and evidently distinct species which is perhaps more easily detected, is not only contrary to scientific procedure, but is unfair to its discoverer and misleading to future investigators. It seems highly probable that if the method of examination of the small intestine at post-mortem by scrapings from the wall be adopted as a regular procedure the small *Isospora hominis*, first seen by Kjellberg, will be re-discovered.

CONCLUSIONS

1. There occur in cats and dogs three species of coccidia of the genus *Isospora*, namely, *Isospora felis* n. sp., *Isospora rivolta* (Grassi, 1879) and *Isospora bigemina* (Stiles, 1891). The last named is a small parasite of the deeper tissues of the villi of the small intestine, and development of the oocyst may be completed in the vertebrate host, while the two former are larger and are parasitic in the epithelium covering the villi, the development of the oocysts not taking place till they have left the body.

2. It is possible, as maintained by Railliet and Lucet, that there are different varieties of *Isospora bigemina*, namely, *I. bigemina* vars. *canis*, *cati* and *putori* from the dog, cat and pole cat, respectively, but there is at present insufficient evidence to justify the conclusion that they are distinct.

3. The large parasite of the 'swift fox,' described by Weidman as a possible variety of *Isospora bigemina*, does not belong to this species, but is more nearly related to *Isospora felis*. If it is a new species, its name will be *Isospora canivecolis*.

4. The complete development of *Isospora felis* in the epithelium is described. A characteristic feature of the intracellular stages is the gregariniform character of the parasite. Schizonts produce, as

a rule, eight merozoites, but sometimes a larger number. The nuclei of the microgametes are the result of repeated division of the original single nucleus of the young microgametocyte. The karyosome appears to be present in all stages of growth of the parasite. The oocyst wall is not completely formed till the parasite has left the cell, and no change in its contents occurs till the oocyst has left the body.

5. The complete development, including schizogony and sporogony, of *Isospora bigemina* takes place in large cells in the internal tissues of the villi, and here the oocyst is formed and completes its development. Its wall is comparatively thin, while that of the sporocyst is relatively thick.

6. The development of the oocyst of *Isospora rivolta* was studied, and this takes place only after it has left the body; as in the case of *Isospora felis*.

7. The parasite described from the interior of the villi of man by Virchow is a small *Isospora* like *Isospora bigemina*. It bears the name *Isospora hominis* (Railliet and Lucet, 1891).

8. For the larger form discovered in the faeces of man during the war, and regarded by Dobell as identical with the small form described by Virchow, the name *Isospora belli* n. sp., is proposed.

9. A coccidium of the genus *Eimeria* is described from the faeces of dogs. This form is remarkable in that the oocysts vary considerably in size. The name *Eimeria canis* n. sp., is proposed for this parasite.

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ADDENDUM

Since the foregoing account of the coccidia of cats and dogs was written, a paper has come to hand by Zapfe dealing with the *Isospora* of dogs in Germany. The form studied appears to be the one of intermediate size mentioned by Reichenow (1921), and which has been identified as *Isospora rivolta*. It was assumed above that the development of *Isospora rivolta* would be found to take place in the intestinal epithelium, and this has been demonstrated by Zapfe. The various stages are very similar to those of *Isospora felis*, but they are correspondingly smaller, as was to be expected from the smaller size of the oocyst. During schizogony from eight to twenty-four merozoites are produced. The infection is as a rule limited to the distal ends of the villi, as in the case of *Isospora felis*. Zapfe regards the parasite as *Isospora bigemina*, and discusses the statements that have been made as to the occurrence of oocysts in the interior of the villi. He inclines to the view that the oocysts are not actually in this situation, but only appear to be there on account of irregularities in the epithelium. It is evident he has not encountered the small form which unquestionably develops in the interior of the villi.

Reference is made to a paper by Pospiech (1919), which the writer has not seen. This author examined the faeces of a large number of dogs, and came to the conclusion that there were actually four types of *Isospora* in cats and dogs. Three of these correspond with the three forms described above. A fourth type, which occurs in both cats and dogs, has an oocyst which varies in size between that of *Isospora bigemina* and *Isospora rivolta*. The dimensions are given as 17 to 18 microns by 14 microns. The size of the sporocyst is 11 by 7.5 microns. The writer has not seen this form in England, and can express no opinion as to whether it is a distinct species. Zapfe also mentions a paper by Bornhauser (1912), who described a coccidium of the liver of dogs. Nöller is quoted as having expressed the opinion that the structures described were

probably not parasites at all. Reichenow (1921) has come to the same conclusion.

A paper by Otten (1923) refers to the separation of oocysts from the faeces of dogs by a saline concentration method.

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EXPLANATION OF PLATE IX

Isospora felis. ($\times 2000$.)

Figs. 1-18. Schizogony.

1. Smallest form in vacuole in epithelial cell showing attachment to surface of vacuole.
2. Slightly larger form with similar attachment.
3. Stage just prior to commencement of nuclear division.
4. Commencing nuclear division. The karyosome in division.
5. Intranuclear spindle showing equatorial plate of chromosomes and daughter karyosomes at ends of spindle.
6. Similar stage showing daughter plates of chromosomes.
7. Stage with two nuclei.
8. Similar stage.
9. Second nuclear division.
10. Stage with four nuclei.
11. Third nuclear division.
12. Stage with eight nuclei. The karyosome is still present though reduced in size.
13. Formation of merozoites from the central cytoplasmic body. Only six of the eight merozoites are shown.
14. Eight merozoites and residual body in vacuole in cell.
15. Eight merozoites of larger size in vacuole.
16. Three merozoites in a vacuole. This is either division into a small number of merozoites or the result of multiple infection.
17. Stage with sixteen merozoites, only fourteen of which appeared in the section.
18. Stage with sixteen larger merozoites.

Figs. 19-28. Growth of microgametocyte.

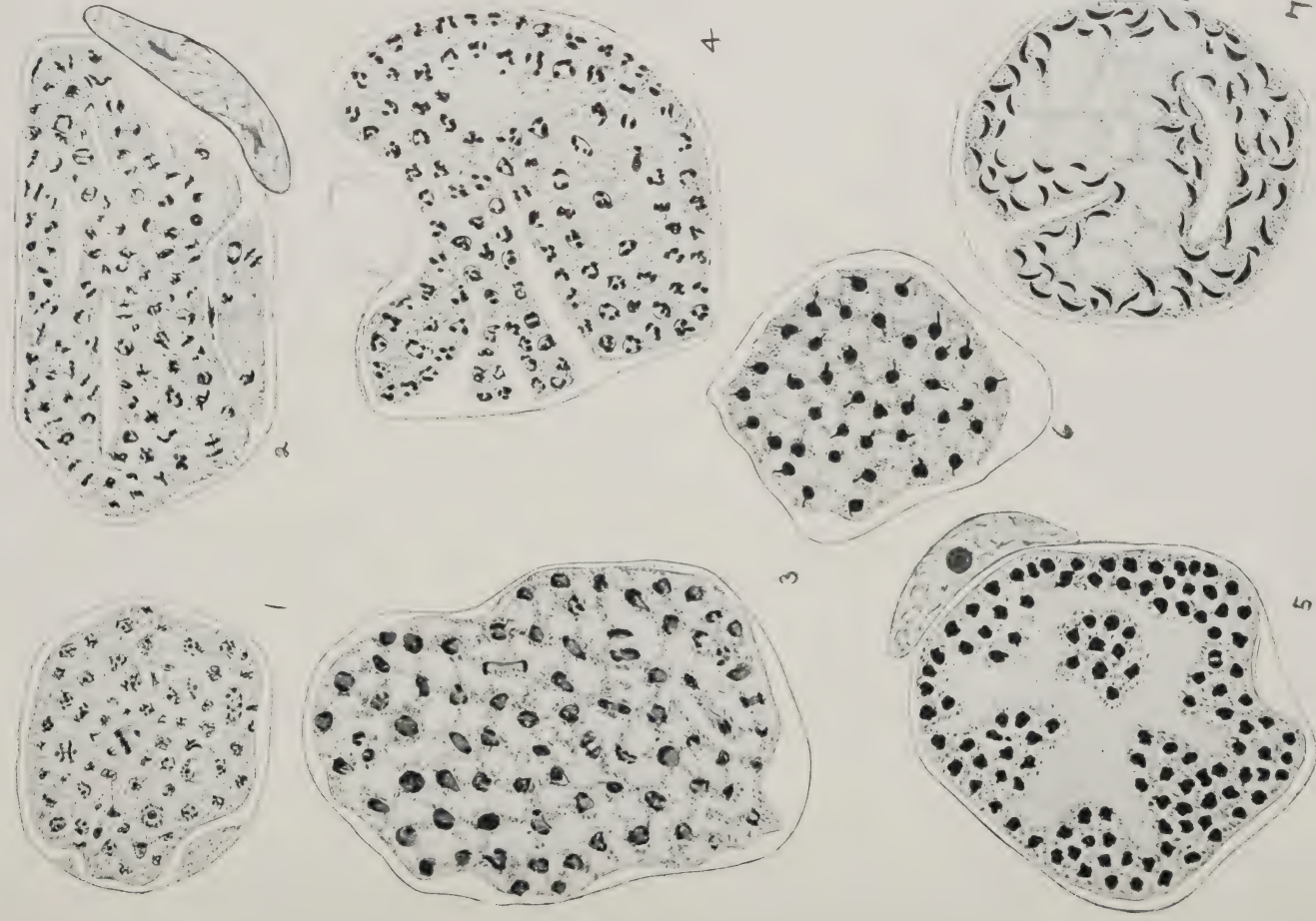
19. Young microgametocyte ?
20. First nuclear division.
21. Similar form.
22. Stage with two nuclei.
23. Stage with four nuclei.
24. Stage with eight nuclei.
25. One section of stage with sixteen nuclei.
26. One section of stage with about thirty-two nuclei.
27. One section of stage with larger number of nuclei, many of which are dividing. The chromosomes can be detected.
28. One section of stage with still larger number of nuclei.



EXPLANATION OF PLATE X

Figs. 1-7. Growth of Microgametocyte (*contd.*)

1. One section of stage in which the chromatin has become more distinct, the cytoplasm clearer and the karyosome smaller. Definite mitotic division of the nuclei is taking place.
2. One section of stage in which the chromatin is still more marked.
3. One section of stage in which the chromatin is much coarser. Some nuclei are showing what is probably the last nuclear division.
4. One section of stage in which the final nuclear division has taken place. Each nucleus includes several coarse chromatin masses. In some an isolated granule can be detected. This may be the karyosome.
5. One section of stage in which the chromatin granules are becoming aggregated into a single mass.
6. One section of stage in which the chromatin of the nuclei has become completely condensed into a single mass and has formed finger-like outgrowths.
7. One section of stage in which the chromatin of the nuclei has assumed a falciform shape.



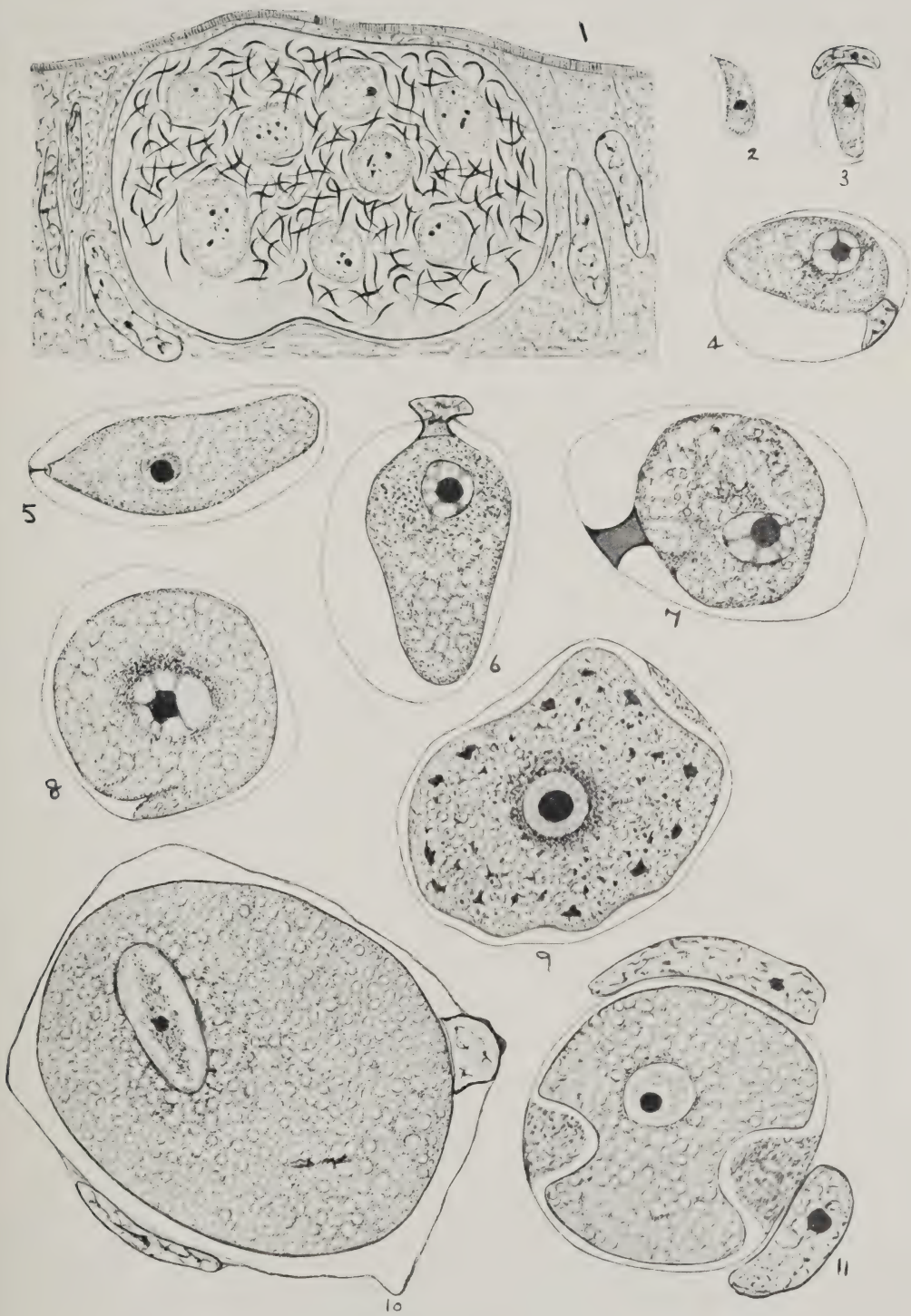
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EXPLANATION OF PLATE XI

Fig. 1. One section of stage in which microgamete formation is completed and several residual bodies are present.

Figs. 2-11. Growth of macrogametocyte.

2. Very young macrogametocyte ?
3. Slightly later stage showing attachment to the surface of the vacuole against the nucleus of the host cell.
4. Later stage showing attachment to the nucleus of the host cell, which has been drawn into the vacuole.
5. Still later stage showing the appearance of a terminal sucker into which a pedicle of the cell cytoplasm has been drawn.
6. Still later stage attached to nucleus.
7. Section of larger form with nucleus of host cell within the vacuole.
8. Section of larger form showing doubled-up condition. The granules of deeply staining material are appearing round the nucleus.
9. Section of later stage. The granules round the nucleus are more marked while deeply staining masses appear in the cytoplasm.
10. Section of larger form. Globules of a refractile substance are appearing in the cytoplasm.
11. Section of a stage in which the globules of refractile substance are more pronounced. The surface is indented in two places by an accumulation of an eosinophile granular material against the wall of the vacuole.



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EXPLANATION OF PLATE XII

Fig. 1. Fully developed stage with clear cytoplasm filled with globules of refractile substance. The oocyst wall is just commencing to form.

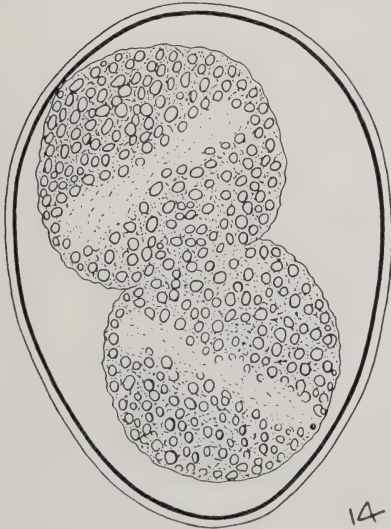
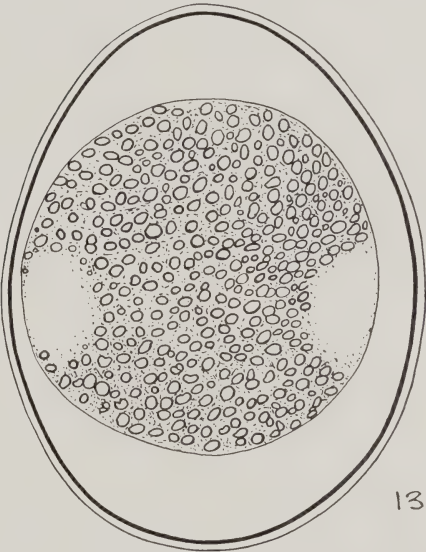
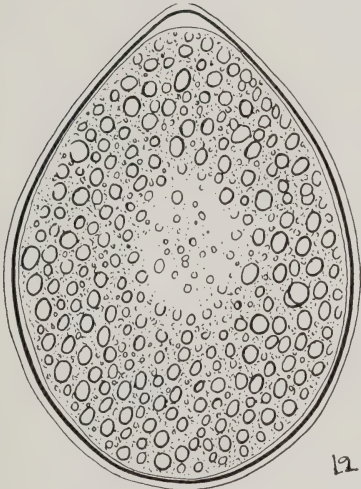
Figs. 2-11. Sporogony.

A small area of cytoplasm is figured round each nucleus in Figs. 2-7.

2. Nucleus of the zygote.
3. Two nuclei in zygote after first nuclear division.
4. First nuclear division in a sporoblast.
5. Two nuclei in a sporoblast.
6. Second nuclear division in a sporoblast.
7. Four nuclei in a sporoblast.
8. Sporozoite showing granule at centre of karyosome.
9. Sporozoite with karyosome more deeply stained.
10. Sporozoite showing vacuole in cytoplasm left by solution of refractile body.
11. Stained sporocyst showing four sporozoites and large residual body.

Figs. 12-15. *Isospora felis*—oocysts as seen in living condition. ($\times 1500$).

12. Condition in which oocyst leaves the body.
13. Oocyst in which the zygote has become spherical and the nucleus divided.
14. Two sporoblasts in which first nuclear division is taking place.
15. Mature oocyst showing two sporocysts, each with four sporozoites and a residual body.



EXPLANATION OF PLATE XIII

Figs. 1-11. *Isospora bigemina*. ($\times 2000$).

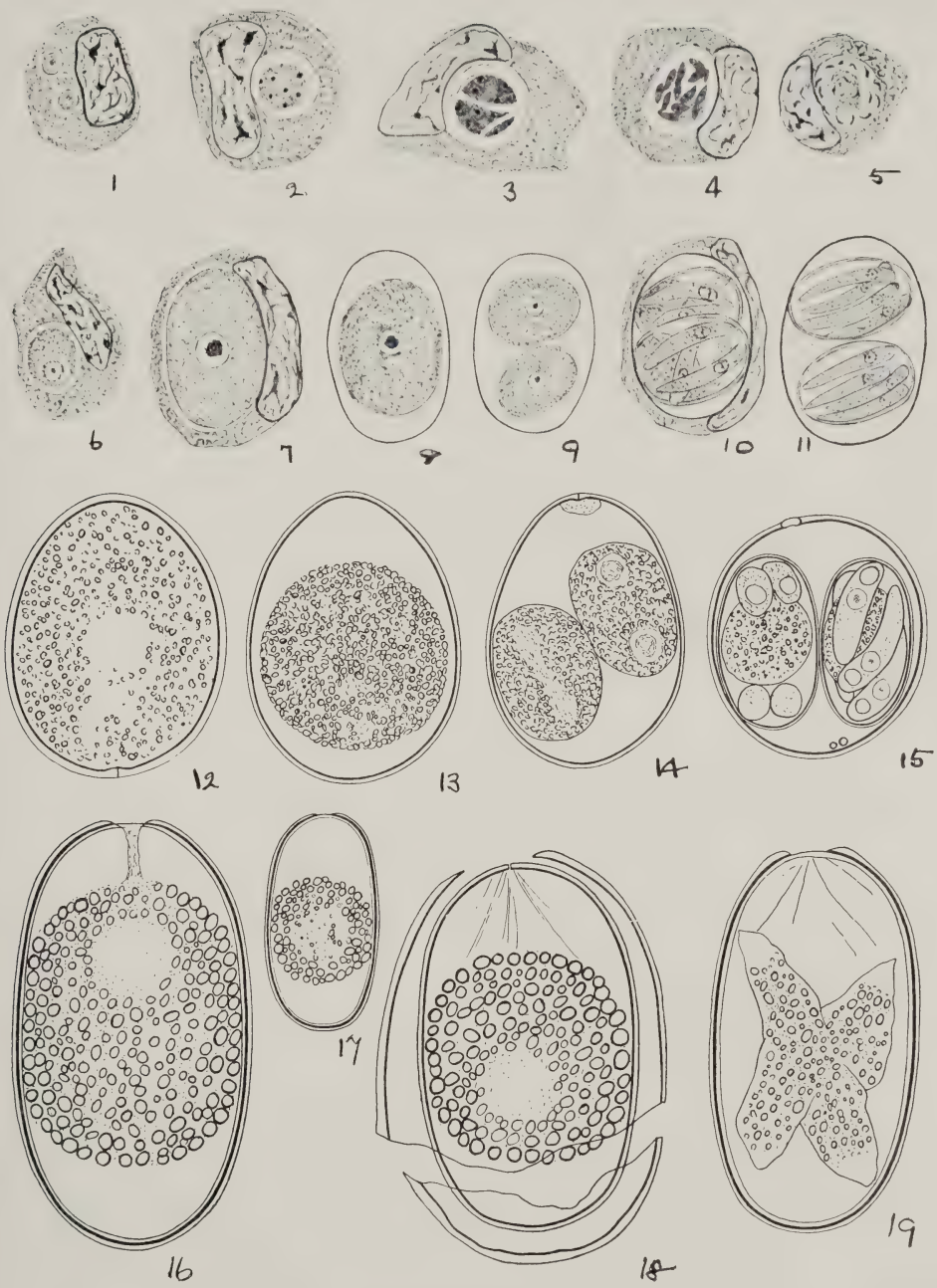
1. Two young schizonts in mononuclear cell.
2. Multinucleated schizont.
3. Commencing segmentation of schizont.
4. One section of stage with about sixteen merozoites.
5. Microgametes and residual body.
6. Partly developed macrogametocyte.
7. Fully grown macrogametocyte.
8. Oocyst with enclosed zygote.
9. Oocyst with two sporoblasts.
10. Fully developed oocyst with two sporocysts, each with four sporozoites and a residual body.
11. Similar stage with no residual body visible in the sporocysts.

Figs. 12-15. *Isospora rivolta*—oocysts as seen in living condition. ($\times 1500$).

12. Condition in which oocyst leaves the body.
13. Oocyst in which zygote has become spherical.
14. Oocyst with two sporoblasts in one of which the nucleus is dividing, while in the other the first nuclear division is complete.
15. Mature oocyst containing fully developed sporocysts.

Figs. 16-19. *Eimeria canis*—oocysts as seen in the living condition. ($\times 1500$).

16. Large oocyst with spherically contracted zygote attached to micropyle by pedicle.
17. Very much smaller oocyst of similar type.
18. Large oocyst with the outer covering breaking away.
19. Oocyst with outer covering intact. The zygote is budding off from sporoblasts as pyramidal bodies.



EXPLANATION OF PLATE XIV

Figs. 1-8. *Eimeria canis*—oocysts as seen in the living condition (*continued*).
($\times 1500$)

1. Oocyst with outer covering intact. Four sporoblasts and a residual body are present.
2. Similar form with four sporoblasts and no residual body.
3. Oocyst with four elongated sporoblasts and a residual body. The outer covering of the oocyst has disappeared except at two small areas.
4. Oocyst in similar stage of development with outer covering intact.
5. Oocyst with outer covering intact and four undeveloped sporocysts and a residual body.
6. Completely developed oocyst with residual body and four sporocysts, each of which has a terminal knob and includes two sporozoites and a residual body.
7. Completely developed oocyst of much smaller size.
8. Similar but slightly smaller oocyst.

